L Number	Hits	Search Text	DB	Time stamp
1	1145931	target or targeting or targeted or bind or binding or bound or recognition	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/18 17:46
7	600368	site or motif or domain	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/18 17:47
13	1634343	variant or exogenous or inserted	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/18 17:50
19	72330	(target or targeting or targeted or bind or binding or bound or recognition) near4 (site or motif or domain)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/18 17:50
25	18358	(site or motif or domain) near4 (variant or exogenous or inserted)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/18 17:51
31	11496	((target or targeting or targeted or bind or binding or bound or recognition) near4 (site or motif or domain)) and ((site or motif or domain) near4 (variant or exogenous or inserted))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/18 17:51
37	4216	(modified or variant)near2 enzyme	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/18 17:52
43	550	(((target or targeting or targeted or bind or binding or bound or recognition) near4 (site or motif or domain)) and ((site or motif or domain) near4 (variant or exogenous or inserted))) and ((modified or variant)near2 enzyme)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/18 17:53
49	163	((((target or targeting or targeted or bind or binding or bound or recognition) near4 (site or motif or domain)) and ((site or motif or domain) near4 (variant or exogenous or inserted))) and ((modified or variant)near2 enzyme)) not fusion	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/18 17:53
55	321	((((target or targeting or targeted or bind or binding or bound or recognition) near4 (site or motif or domain)) and ((site or motif or domain) near4 (variant or exogenous or inserted))) and ((modified or variant)near2 enzyme)) NOT (fusion adj protein)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/18 17:54
61	36	(((((target or targeting or targeted or bind or binding or bound or recognition) near4 (site or motif or domain)) and ((site or motif or domain) near4 (variant or exogenous or inserted))) and ((modified or variant)near2 enzyme)) not fusion) and lactamase	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/18 17:54

Swope 10/022,073

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FILE COVERS 1907 - 18 Mar 2003  VOL 138 ISS 12
FILE LAST UPDATED: 17 Mar 2003  (20030317/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d que l9
L1          568 SEA FILE=REGISTRY LACTAMASE?/CN
L2          561 SEA FILE=REGISTRY BETA(3A)LACTAMASE?/CN
L3          568 SEA FILE=REGISTRY L1 OR L2
L5          101 SEA FILE=REGISTRY VHKTGSTG/SQSP
L7           33 SEA FILE=REGISTRY L3 AND L5
L9           18 SEA FILE=HCAPLUS L7


=> d ibib abs l9 1-18

L9   ANSWER 1 OF 18  HCAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2002:840894  HCAPLUS
DOCUMENT NUMBER:          138:150012
TITLE:                    Characterization of CMY-type .beta.-lactamases in
                          clinical strains of Proteus mirabilis and Klebsiella
                          pneumoniae isolated in four hospitals in the Paris
                          area
AUTHOR(S):                Decre, Dominique; Verdet, Charlotte; Raskine, Laurent;
                          Blanchard, Herve; Burghoffer, Beatrice; Philippon,
                          Alain; Sanson-Le-Pors, Marie Jose; Petit, Jean Claude;
                          Arlet, Guillaume
CORPORATE SOURCE:         Hopital Saint Antoine, Service de Bacteriologie, UFR
                          Saint-Antoine, Paris, 75012, Fr.
SOURCE:                   Journal of Antimicrobial Chemotherapy (2002), 50(5),
                          681-688
                          CODEN: JACHDX; ISSN: 0305-7453
PUBLISHER:                Oxford University Press
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   We isolated 5 clin. strains (3 P. mirabilis and 2 K. pneumoniae) with
     .beta.-lactam resistance phenotypes consistent with prodn. of an AmpC-type
     .beta.-lactamase.  The predicted amino acid sequences of the enzymes were
     typical of class C .beta.-lactamases.  The enzymes were identified as
     CMY-2, CMY-4 and a new CMY-variant .beta.-lactamase, CMY-12.  The AmpC
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.beta.-lactamases from the 2 K. pneumoniae isolates were found to be encoded on self-transferable plasmids. The genes encoding the AmpC-type .beta.-lactamase produced by the 3 P. mirabilis isolates were chromosomal. Four of the 5 clin. isolates were from patients transferred from Greece, Algeria, and Egypt; 1 of the K. pneumoniae strains was recovered from a French patient. PFGE anal. and rep-PCR fingerprinting showed that the 2 P. mirabilis isolates from Greek patients were closely related.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 18 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:806911 HCAPLUS
DOCUMENT NUMBER: 138:118276
TITLE: Cloning and sequencing of the .beta.-lactamase gene and surrounding DNA sequences of Citrobacter braakii, Citrobacter murliniae, Citrobacter werkmanii, Escherichia fergusonii and Enterobacter cancerogenus
AUTHOR(S): Naas, Thierry; Aubert, Daniel; Fortineau, Nicolas; Nordmann, Patrice
CORPORATE SOURCE: Faculte de Medecine Paris-Sud, Assistance Publique-Hopitaux de Paris, Hospital de Bicetre, Hospital de Bicetre, Paris, 94275, Fr.
SOURCE: FEMS Microbiology Letters (2002), 215(1), 81-87
CODEN: FMLED7; ISSN: 0378-1097
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To further identify the origins of plasmid-mediated cephalosporinases that are currently spreading worldwide, the chromosomal .beta.-lactamase genes of Citrobacter braakii, Citrobacter murliniae, Citrobacter werkmanii ref. strains and of Escherichia fergusonii and Enterobacter cancerogenus clin. isolates were cloned and expressed into Escherichia coli and sequenced. These .beta.-lactamases had all a single pI value >8 and conferred a typical AmpC-type resistance pattern in E. coli recombinant strains. The cloned inserts obtained from genomic DNAs of each strain encoded Ambler class C .beta.-lactamases. The AmpC-type enzymes of C. murliniae, C. braakii and C. werkmanii shared 99%, 96% and 95% amino acid sequence identity, resp., with chromosomal AmpC .beta.-lactamases from Citrobacter freundii. The AmpC-type enzyme of E. cancerogenus shared 85% amino acid sequence identity with the chromosomal AmpC .beta.-lactamase of Enterobacter cloacae OUDhyp and the AmpC-type enzyme of E. fergusonii shared 96% amino acid sequence identity with that of E. coli K12. The ampC genes, except for E. fergusonii, were assocd. with genes homologous to regulatory ampR genes of other chromosomal class C .beta.-lactamases that explain inducibility of .beta.-lactamase expression in these strains. This work provides further evidence of the mol. heterogeneity of class C .beta.-lactamases.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:465839 HCAPLUS
DOCUMENT NUMBER: 137:52345
TITLE: Targeted enzyme prodrug therapy
INVENTOR(S): Schellenberger, Volker
PATENT ASSIGNEE(S): Genencor International, USA
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

Search completed by David Schreiber 308-4292

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002047717	A2	20020620	WO 2001-US48529	20011214
W: AL, AM, AU, AZ, BB, BG, CA, CH, CN, CR, DE, DK, DM, DZ, EE, ES, FI, HU, ID, IL, IN, JP, KE, KP, LC, LT, LU, MK, MN, SD, SE, SG, SI, SK, SL, TM, TR, UA, UG, US, YU, ZA, RU, TJ, TM				
RW: GH, GM, LS, SD, TZ, AT, BE, CY, DE, FI, FR, IE, IT, LU, CF, CG, GA, ML, NE, SN, TD, TG				
AU 2002030890	A5	20020624	AU 2002-30890	20011214

PRIORITY APPLN. INFO.: US 2000-255774P P 20001214
US 2001-279609P P 20010328
WO 2001-US48529 W 20011214

AB The present invention provides targeting enzymes that bind to targets better than the corresponding pre-targeting enzymes bind the target under like conditions, methods of making targeting enzymes, methods of using targeting enzymes to treat diseases, and pharmaceutical compns. comprising targeting enzymes.

L9 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:383250 HCAPLUS
DOCUMENT NUMBER: 137:227310
TITLE: Chromosomal ampC genes in Enterobacter species other than Enterobacter cloacae, and ancestral association of the ACT-1 plasmid-encoded cephalosporinase to Enterobacter asburiae
AUTHOR(S): Rottman, Martin; Benzerara, Yahia; Hanau-Bercot, Beatrice; Bizet, Chantal; Philippon, Alain; Arlet, Guillaume
CORPORATE SOURCE: Service de Bacteriologie, Hopital Tenon, UFR Saint Antoine, Paris, Fr.
SOURCE: FEMS Microbiology Letters (2002), 210(1), 87-92
CODEN: FMLED7; ISSN: 0378-1097
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The amplification and sequence of ampC genes in Enterobacter asburiae, Enterobacter cancerogenus, Enterobacter dissolvens, Enterobacter hormaechei and Enterobacter intermedius bring the no. of known cephalosporinase sequences from the genus Enterobacter to seven. Expression in Escherichia coli of the ampC genes from E. asburiae, E. hormaechei and E. intermedius established the functional nature of these genes. ampC from E. asburiae shows 96.5% identity to blaACT-1 encoding a plasmid-borne cephalosporinase previously believed to derive from Enterobacter cloacae. The reassignment of ACT-1 ancestry to E. asburiae is confirmed by the 95.5% identity between ampR upstream of blaACT-1 and ampR from E. asburiae.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:868669 HCAPLUS
DOCUMENT NUMBER: 136:15894
TITLE: Methods involving identification and use of sites for gene recombination in biopolymer engineering
INVENTOR(S): Wang, Zhen-Gang; Voigt, Christopher A.; Mayo, Stephen

L.; Arnold, Frances H.
PATENT ASSIGNEE(S): California Institute of Technology, USA
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001090346	A2	20011129	WO 2001-US16831	20010523
WO 2001090346	A3	20021010		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1283877	A2	20030219	EP 2001-937702	20010523

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:

US 2000-207048P	P	20000523
US 2000-235960P	P	20000927
US 2001-283567P	P	20010413
WO 2001-US16831	W	20010523

AB The invention relates to improved methods for directed evolution of polymers, including directed evolution of nucleic acids and proteins. Specifically, the methods of the invention include anal. methods for identifying "crossover locations" in a polymer. Crossovers at these locations are less likely to disrupt desirable properties of the protein, such as stability or functionality. The invention further provides improved methods for directed evolution wherein the polymer is selectively recombined at the identified "crossover locations". Crossover disruption profiles can be used to identify preferred crossover locations. Structural domains of a biopolymer can also be identified and analyzed, and domains can be organized into schema. Schema disruption profiles can be calcd., for example based on conformational energy or interat. distances, and these can be used to identify preferred or candidate crossover locations. Computer systems for implementing anal. methods of the invention are also provided. Examples of the invention include computational calcns. of regions of .beta.-lactamase in which crossovers/in vitro recombination would disrupt protein structure, calcns. of a probability distribution for disruption of protein (sub)structures of computationally-generated recombinant mutants, and comparison of a predicted protein disruption profile with exptl. obsd. recombination crossover points.

L9 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:380170 HCAPLUS
DOCUMENT NUMBER: 135:149010
TITLE: Characterization of an extended-spectrum class C .beta.-lactamase of Citrobacter freundii
AUTHOR(S): Haruta, Shin; Nukaga, Michiyoshi; Sawai, Tetsuo
CORPORATE SOURCE: Division of Microbial Chemistry, Faculty of Pharmaceutical Sciences, Chiba University, Chiba,

Chiba, 263-8522, Japan
SOURCE: Microbiology and Immunology (2001), 45(4), 277-283
CODEN: MIIMDV; ISSN: 0385-5600
PUBLISHER: Center for Academic Publications Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Citrobacter freundii GC3 is a clin. isolate which showed moderate resistance to oxyimino .beta.-lactams such as ceftazidime and aztreonam. This drug resistance was due to an extended-spectrum class C .beta.-lactamase encoded by chromosomal gene(s). The GC3 .beta.-lactamase showed high amino acid sequence homol. to a known C. freundii .beta.-lactamase, i.e., 346 of 361 amino acids were identical with those of C. freundii GN346 .beta.-lactamase. Asp198 was the only dissimilar amino acid found in the omega loop region, known as the hot spot for extended-spectrum resistance in class C .beta.-lactamases. However, Asp198 was eliminated as a cause of the extended-spectrum resistance by the substitution of Asn for Asp198. Subsequent investigation suggested that the moderate resistance to oxyimino .beta.-lactams is attributable to the replacement of amino acids on the enzyme's surface area, far from the active-site. Some or all of the replacements are assumed to delicately modify the active-site configuration. The GC3 .beta.-lactamase is the first example of an extended-spectrum class C .beta.-lactamase in which mutations are independent of the omega loop.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:110775 HCAPLUS
DOCUMENT NUMBER: 134:323315

TITLE: Extension of resistance to cefepime and cefpirome associated to a six amino acid deletion in the H-10 helix of the cephalosporinase of an Enterobacter cloacae clinical isolate

AUTHOR(S): Barnaud, G.; Labia, R.; Raskine, L.; Sanson-Le Pors, M. J.; Philippon, A.; Arlet, G.
CORPORATE SOURCE: Service de Bacteriologie-Virologie, Hopital Lariboisiere, Paris, 75475, Fr.

SOURCE: FEMS Microbiology Letters (2001), 195(2), 185-190
CODEN: FMLED7; ISSN: 0378-1097
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Enterobacter cloacae CHE, a clin. strain with overproduced cephalosporinase was found to be highly resistant to the new cephalosporins, cefepime and cefpirome (MICs.gtoreq.128 .mu.g ml-1). The strain was isolated from a child previously treated with cefepime. The catalytic efficiency of the purified enzyme with the third-generation cephalosporins, cefepime and cefpirome, was 10 times higher than that with the E. cloacae P99 enzyme. This was mostly due to a decrease in Km for these .beta.-lactams. The clin. isolate produced large amts. of the cephalosporinase because introduction of the ampD gene decreased ampC expression and partially restored the wild-type phenotype. Indeed, MICs of cefepime and cefpirome remained 10 times higher than those for a stable derepressed clin. isolate (OUDhyp) transformed with an ampD gene. Sequencing of the ampC gene showed that 18 nucleotides had been deleted, corresponding to the six amino acids SKVALA (residues 289-294). According to the crystal structure of P99 .beta.-lactamase, this deletion was located in the H-10 helix. The ampR-ampC genes from the clin. isolates CHE and OUDhyp were cloned and expressed in Escherichia coli JM101. The

MICs of cefpirome and cefepime of E. coli harboring ampC and ampR genes from CHE were 100-200 times higher than those of E. coli harboring ampC and ampR genes from OUDhyp. This suggests that the deletion, confirmed by sequencing of the ampC gene, is involved in resistance to cefepime and cefpirome. However, the high level of resistance to cefepime and cefpirome obsd. in the E. cloacae clin. isolate was due to a combination of hyperprodn. of the AmpC .beta.-lactamase and structural modification of the enzyme. This is the first example of an AmpC variant conferring resistance to cefepime and cefpirome, isolated as a clin. strain.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:780120 HCAPLUS
DOCUMENT NUMBER: 134:276363
TITLE: Nucleotide sequence of the chromosomal ampC gene of Enterobacter aerogenes
AUTHOR(S): Preston, Karen E.; Radomski, Christopher C. A.; Venezia, Richard A.
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Albany Medical Center Hospital, Albany, NY, 12208, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(11), 3158-3162
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The AmpC .beta.-lactamase gene and a small portion of the regulatory ampR sequence of Enterobacter aerogenes 97B were cloned and sequenced. The .beta.-lactamase had an isoelec. point of 8 and conferred cephalosporin and cephamycin resistance on the host. The sequence of the cloned gene is most closely related to those of the ampC genes of E. cloacae and C. freundii.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:434740 HCAPLUS
DOCUMENT NUMBER: 131:195156
TITLE: Sequence of the MIR-1 .beta.-lactamase gene
AUTHOR(S): Jacoby, George A.; Tran, John
CORPORATE SOURCE: Edith Nourse Rogers Memorial Veterans Hospital, Bedford, MA, 01730, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1999), 43(7), 1759-1760
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The complete nucleotide sequence of the plasmid-mediated MIR-1 .beta.-lactamase gene confirms its relationship to chromosomally located ampC genes of Enterobacter cloacae. BlaMIR-1 is not part of a typical gene cassette but does lie near an element that could be involved in its capture on a plasmid.
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:369415 HCAPLUS

Search completed by David Schreiber 308-4292

Swope 10/022,073

DOCUMENT NUMBER: 131:154340
TITLE: Characterization and nucleotide sequence of a Klebsiella oxytoca cryptic plasmid encoding a CMY-type .beta.-lactamase: confirmation that the plasmid-mediated cephamycinase originated from the Citrobacter freundii AmpC .beta.-lactamase
AUTHOR(S): Wu, Shang Wei; Dornbusch, Kathrine; Kronvall, Goran; Norgren, Mari
CORPORATE SOURCE: Department of Laboratory Medicine, Division of Clinical Microbiology, Karolinska Institute and Karolinska Hospital, Stockholm, 171 76, Swed.
SOURCE: Antimicrobial Agents and Chemotherapy (1999), 43(6), 1350-1357
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Plasmid pTKH11, originally obtained by electroporation of a Klebsiella oxytoca plasmid prepn. into Escherichia coli XAC, expressed a high level of an AmpC-like .beta.-lactamase. The enzyme, designated CMY-5, conferred resistance to extended-spectrum .beta.-lactams in E. coli; nevertheless, the phenotype was cryptic in the K. oxytoca donor. Detn. of the complete nucleotide sequence of pTKH11 revealed that the 8193-bp plasmid encoded seven open reading frames, including that for the CMY-5 .beta.-lactamase (blaCMY-5). The blaCMY-5 product was similar to the plasmidic CMY-2 .beta.-lactamase of K. pneumoniae and the chromosomal AmpC of Citrobacter freundii, with 99.7 and 97.0% identities, resp.; there was a substitution of phenylalanine in CMY-5 for isoleucine 105 in CMY-2. BlaCMY-5 was followed by the Blc and SugE genes of C. freundii, and this cluster exhibited a genetic organization identical to that of the ampC region on the chromosome of C. freundii; these results confirmed that C. freundii AmpC was the evolutionary origin of the plasmidic cephamycinases. In the K. oxytoca host, the copy no. of pTKH11 was very low and the plasmid coexisted with plasmid pNBL63. Anal. of the replication regions of the two plasmids revealed 97% sequence similarity in the RNA I transcripts; this result implied that the two plasmids might be incompatible. Incompatibility of the two plasmids might explain the cryptic phenotype of blaCMY-5 in K. oxytoca through an exclusion effect on pTKH11 by resident plasmid pNBL63.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:303022 HCAPLUS
DOCUMENT NUMBER: 131:99761
TITLE: Carbapenem resistance in Escherichia coli associated with plasmid-determined CMY-4 .beta.-lactamase production and loss of an outer membrane protein
AUTHOR(S): Stapleton, Paul D.; Shannon, Kevin P.; French, Gary L.
CORPORATE SOURCE: Department of Microbiology, UMDS, St. Thomas' Hospital, London, UK
SOURCE: Antimicrobial Agents and Chemotherapy (1999), 43(5), 1206-1210
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three cefoxitin-resistant Escherichia coli isolates from stool specimens of a patient with leukemia were either resistant, intermediate, or

Search completed by David Schreiber 308-4292

sensitive to imipenem. Conjugation expts. showed that cefoxitin resistance, but not imipenem resistance, was transferable. All isolates were shown by isoelec. focusing to produce two .beta.-lactamases with isoelec. points of 5.4 (TEM-1, confirmed by sequencing of a PCR product) and >8.5 (consistent with a class C .beta.-lactamase). The gene coding for the unknown .beta.-lactamase was cloned and sequenced and revealed an enzyme which had 99.9% sequence identity with the plasmid-detd. class C .beta.-lactamase CMY-2. The cloned .beta.-lactamase gene differed from blaCMY-2 at one nucleotide position that resulted in an amino acid change, tryptophan to arginine at position 221. We propose that this enzyme be designated CMY-4. Both the imipenem-resistant and -intermediate isolates lacked a 38-kDa outer membrane protein (OMP) that was present in the imipenem-sensitive isolate. The lack of an OMP alone did not explain the difference in carbapenem susceptibilities obsd. However, measurement of .beta.-lactamase activities (including measurements under conditions where TEM-1 .beta.-lactamase was inhibited) indicated that the imipenem-intermediate isolate expressed six- to eightfold less .beta.-lactamase than did the other isolates. This study illustrates that carbapenem resistance in E. coli can arise from high-level expression of plasmid-mediated class C .beta.-lactamase combined with an OMP deficiency. Furthermore, in the presence of an OMP deficiency, the level of expression of a plasmid-mediated class C .beta.-lactamase is an important factor in detg. whether E. coli isolates are fully resistant to carbapenems.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:156274 HCAPLUS
DOCUMENT NUMBER: 126:248720
TITLE: Imipenem resistance in Klebsiella pneumoniae is associated with the combination of ACT-1, a plasmid-mediated AmpC .beta.-lactamase, and the loss of an outer membrane protein
AUTHOR(S): Bradford, Patricia A.; Urban, Carl; Mariano, Noriel; Projan, Steven J.; Rahal, James J.; Bush, Karen
CORPORATE SOURCE: Wyeth-Ayerst Res., Pearl River, NY, 10965, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1997), 41(3), 563-569
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Six Escherichia coli and 12 K. pneumoniae isolates from a single hospital expressed a common .beta.-lactamase with a pI of .apprx.9.0 and were resistant to cefoxitin and cefotetan (MIC ranges, 64 to >128 and 16 to >128 .mu.g/mL, resp.). Seventeen of the 18 strains produced multiple .beta.-lactamases. Most significantly, 3 K. pneumoniae strains were also resistant to imipenem (MICs, 8-32 .mu.g/mL). Spectrophotometric .beta.-lactamase assays with purified enzyme indicated hydrolysis of cephamycins, in addn. to cephaloridine and benzylpenicillin. The gene encoding the pI 9.0 .beta.-lactamase (designated ACT-1 for AmpC type) was cloned and sequenced, which revealed an ampC-type .beta.-lactamase gene that originated from Enterobacter cloacae and that had 86% sequence homol. to the P99 .beta.-lactamase and 94% homol. to the partial sequence of MIR-1. Southern blotting revealed that the gene encoding ACT-1 was on a large plasmid in some of the K. pneumoniae strains as well as on the chromosomes of all of the strains, suggesting that the gene is located on an easily mobilized element. Outer membrane protein profiles of the K. pneumoniae strains revealed that the 3 imipenem-resistant strains were

lacking a major outer membrane protein of .apprx.42 kDa which was present in the imipenem-susceptible strains. ACT-1 is the 1st plasmid-mediated AmpC-type .beta.-lactamase derived from Enterobacter which has been completely sequenced. This work demonstrates that in addn. to resistance to cephamycins, imipenem resistance can occur in K. pneumoniae when a high level of the ACT-1 .beta.-lactamase is produced in combination with the loss of a major outer membrane protein.

L9 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:19731 HCAPLUS
DOCUMENT NUMBER: 124:139606
TITLE: Characterization of the plasmidic .beta.-lactamase CMY-2, which is responsible for cephamycin resistance
AUTHOR(S): Bauernfeind, A.; Stemplinger, I.; Jungwirth, R.; Giamarellou, H.
CORPORATE SOURCE: Max von Pettenkofer-Inst., Munich, Germany
SOURCE: Antimicrobial Agents and Chemotherapy (1996), 40(1), 221-4
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The phenotype of Klebsiella pneumoniae HEL-1 indicates a plasmidic cephamycinase gene (blaCMY-2). Its sequence shows one open reading frame coding for a protein of 381 amino acids. CMY-2 is classified as class C .beta.-lactamase that is closely related to the plasmidic enzymes BIL-1 and LAT-1 and the chromosomal AmpC of Citrobacter freundii. The blaCMY-2 gene possibly was translocated onto a plasmid of C. freundii which spread to K. pneumoniae.

L9 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:796654 HCAPLUS
DOCUMENT NUMBER: 124:108034
TITLE: Molecular evolution of a class C .beta.-lactamase extending its substrate specificity. [Erratum to document cited in CA123:189958]
AUTHOR(S): Nukaga, Michiyoshi; Haruta, Shin; Tanimoto, Kyoko; Kogure, Keiko; Taniguchi, Kazuo; Tamaki, Mami; Sawai, Tesuo
CORPORATE SOURCE: Fac. Pharmaceutical Sciences, Chiba Univ., Chiba, 263, Japan
SOURCE: Journal of Biological Chemistry (1995), 270(36), 21428
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Bio logy
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The errors were not reflected in the abstr. or the index entries.

L9 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:444428 HCAPLUS
DOCUMENT NUMBER: 123:189958
TITLE: Molecular evolution of a class C .beta.-lactamase extending its substrate specificity
AUTHOR(S): Nukaga, Michiyoshi; Haruta, Shin; Tanimoto, Kyoko; Kogure, Keiko; Taniguchi, Kazuo; Tamaki, Mami; Sawai, Tetsuo
CORPORATE SOURCE: Fac. Pharmaceutical Sciences, Chiba Univ., Chiba, 263, Japan

Search completed by David Schreiber 308-4292

SOURCE: Journal of Biological Chemistry (1995), 270(11), 5729-35
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Enterobacter cloacae GC1, a clin. strain isolated in 1992 in Japan, was found to produce a chromosomal class C .beta.-lactamase with extended substrate specificity to oxyimino .beta.-lactam antibiotics, significantly differing from the known E. cloacae .beta.-lactamases such as the P99 .beta.-lactamase. The 1560 nucleotides including the GC1 .beta.-lactamase gene were sequenced, and the amino acid sequence of the mature enzyme comprising 364 amino acids was deduced. A comparison of the amino acid sequence with those of known E. cloacae .beta.-lactamases revealed the duplication of three amino acids at positions 208-213, i.e. Ala-Val-Arg-Ala-Val-Arg. This duplication was attributed to a tandem duplication of a 9-nucleotide sequence. The chimeric .beta.-lactamases produced by the chimeric genes from the GC1 and P99 .beta.-lactamase genes indicated that the extended substrate specificity is entirely attributed to the 3-amino acid insertion. Two mutant .beta.-lactamases were prepd. from P99 .beta.-lactamase by site-directed mutagenesis, i.e. and Ala-Ala-Ala sequence was inserted before or after the native Ala-Val-Arg at positions 208-210. These mutant enzymes revealed that the Ala-Val-Arg located from positions 211 to 213 in the GC1 .beta.-lactamase are the newly inserted residues, and this phenomenon is independent of the characteristics of the amino acids inserted.

L9 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1994:474868 HCAPLUS
DOCUMENT NUMBER: 121:74868
TITLE: Cloning and sequence analysis of blaBIL-1, a plasmid-mediated class C .beta.-lactamase gene in Escherichia coli BS
AUTHOR(S): Fosberry, Andrew P.; Payne, David J.; Lawlor, Elizabeth J.; Hodgson, John E.
CORPORATE SOURCE: SmithKline Beecham Pharm., Betchworth/Surrey, RH3 7AJ, UK
SOURCE: Antimicrobial Agents and Chemotherapy (1994), 38(5), 1182-5
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The extended-spectrum, plasmid-borne .beta.-lactamase gene blaBIL-1, which was discovered in Escherichia coli, has been cloned. Unusually for a plasmid-borne .beta.-lactamase, blaBIL-1 encodes a novel class C enzyme and appears to have originated from the chromosomal ampC gene of Citrobacter freundii.

L9 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1988:564426 HCAPLUS
DOCUMENT NUMBER: 109:164426
TITLE: Sequence and comparative analysis of three Enterobacter cloacae ampC .beta.-lactamase genes and their products
AUTHOR(S): Galleni, Moreno; Lindberg, Frederik; Normark, Staffan; Cole, Stewart; Honore, Nadine; Joris, Bernard; Frere, Jean Marie
CORPORATE SOURCE: Inst. Chim., Univ. Liege, Sart Tilman/Liege, B-4000,

Belg.
SOURCE: Biochemical Journal (1988), 250(3), 753-60
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The sequences of 3 E. cloacae ampC .beta.-lactamase genes were detd. The deduced amino acid sequences are very similar: of a total of 361 residues, only 8 positions were variable, and several mutations yielded residues with very similar properties. The kinetic properties of 2 of the enzymes were not significantly different. The 3 enzymes also exhibited a high degree of homol. (>70%) with the ampC .beta.-lactamases of Escherichia coli K12 and Citrobacter freundii, confirming the homogeneity of class-C .beta.-lactamases.

L9 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:419585 HCAPLUS
DOCUMENT NUMBER: 105:19585
TITLE: Sequence of the Citrobacter freundii OS60 chromosomal ampC .beta.-lactamase gene
AUTHOR(S): Lindberg, Frederik; Normark, Staffan
CORPORATE SOURCE: Dep. Microbiol., Univ. Umea, Umea, S-901 87, Swed.
SOURCE: European Journal of Biochemistry (1986), 156(3), 441-5
CODEN: EJBCAI; ISSN: 0014-2956
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The C. freundii OS60 ampC .beta.-lactamase [9073-60-3] gene was sequenced and found to encode a 380-amino-acid precursor with a 19-residue signal peptide. The mature protein has a predicted mol. mass of 39,781 daltons. The 1st 60 residues of the purified enzyme, as detd. by sequential Edman degrdn., are identical to the amino acid sequence inferred from the gene sequence. Also, the amino acid compn. detd. for the purified .beta.-lactamase and that given by the gene sequence are in good agreement. The C. freundii and Escherichia coli K12 chromosomal AmpC .beta.-lactamases were identical at 77% of the amino acid positions. This clearly puts the C. freundii enzyme into the class C of .beta.-lactamases. Of the 68 N-terminal residues detd. for the Enterobacter cloacae P99 .beta.-lactamase, 44 are identical to the corresponding residues of the C. freundii enzyme. All 3 enzymes, as well as that of Pseudomonas aeruginosa 18S/H are highly similar around the active-site serine at position 64 of the mature protein.

=> d que l11
L1 568 SEA FILE=REGISTRY LACTAMASE?/CN
L2 561 SEA FILE=REGISTRY BETA(3A)LACTAMASE?/CN
L3 568 SEA FILE=REGISTRY L1 OR L2
L4 119566 SEA FILE=REGISTRY KT.S/SQSP
L5 101 SEA FILE=REGISTRY VHKTGSTG/SQSP
L6 173 SEA FILE=REGISTRY L3 AND L4
L7 33 SEA FILE=REGISTRY L3 AND L5
L8 115 SEA FILE=HCAPLUS L6
L9 18 SEA FILE=HCAPLUS L7
L10 71 SEA FILE=HCAPLUS L8 NOT PY>2000
L11 60 SEA FILE=HCAPLUS L10 NOT L9

=> d ibib abs l11 1-60

L11 ANSWER 1 OF 60 HCAPLUS COPYRIGHT 2003 ACS

Search completed by David Schreiber 308-4292

ACCESSION NUMBER: 2000:845519 HCAPLUS
DOCUMENT NUMBER: 135:56806
TITLE: Aeromonas hydrophila AmpH and CepH .beta.-lactamases: derepressed expression in mutants of Escherichia coli lacking creB
AUTHOR(S): Avison, Matthew B.; Niumsup, Pannika; Walsh, Timothy R.; Bennett, Peter M.
CORPORATE SOURCE: Bristol Centre for Antimicrobial Research and Evaluation (BCARE), Department of Pathology and Microbiology, School of Medical Sciences, University of Bristol, Bristol, BS8 1TD, UK
SOURCE: Journal of Antimicrobial Chemotherapy (2000), 46(5), 695-702
CODEN: JACHDX; ISSN: 0305-7453
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The class 1 cephalosporinase (CepH) and class 2d oxacillinase (AmpH) from an Aeromonas hydrophila clin. isolate, strain T429125, have been cloned and sequenced. Both enzymes are typical of their equiv. in other species of Aeromonas. Both cloned .beta.-lactamase genes were expressed at a low level in a std. lab. Escherichia coli strain, but when cloned into a cre deletion E. coli mutant, they were expressed at significantly higher levels. Specific disruption of the creB gene resulted in similar increased levels of .beta.-lactamase expression, so it was concluded that CreB represses the transcription of ampH and cepH in a cre+ E. coli strain. The expression of cepH was four times that of ampH in the .DELTA.cre mutant because of an addnl. factor encoded on the cloned T429125 chromosomal fragment contg. cepH. This factor was able to trans-activate expression of co-resident ampH in the .DELTA.cre mutant such that expression of the two genes was approx. equal. The entire cepH-contg. fragment was sequenced, but it contained no genes that were obviously related to any known class of DNA-binding protein.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:780138 HCAPLUS
DOCUMENT NUMBER: 134:53753
TITLE: Heterogeneity of AmpC cephalosporinases of Hafnia alvei clinical isolates expressing inducible or constitutive ceftazidime resistance phenotypes
AUTHOR(S): Girlich, Delphine; Naas, Thierry; Bellais, Samuel; Poirel, Laurent; Karim, Amal; Nordmann, Patrice
CORPORATE SOURCE: Service de Bacteriologie-Virologie, Hopital de Bicetre, Assistance Publique/Hopitaux de Paris, Faculte de Medecine Paris-Sud, Le Kremlin-Bicetre, 94275, Fr.
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(11), 3220-3223
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ten unrelated H. alvei clin. isolates were grouped according to either their low-level and inducible cephalosporinase prodn. or their high-level and constitutive cephalosporinase prodn. phenotype. Their AmpC sequences shared 85-100% amino acid identity. The immediate genetic environment of ampC genes was conserved in H. alvei isolates but was different from that

found spp.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:780098 HCAPLUS
DOCUMENT NUMBER: 134:82589
TITLE: SME-type carbapenem-hydrolyzing class A .beta.-lactamases from geographically diverse Serratia marcescens strains
AUTHOR(S): Queenan, Anne Marie; Torres-Viera, Carlos; Gold, Howard S.; Carmeli, Yehuda; Eliopoulos, George M.; Moellering, Robert C., Jr.; Quinn, John P.; Hindler, Janet; Medeiros, Antone A.; Bush, Karen
CORPORATE SOURCE: The R. W. Johnson Pharmaceutical Research Institute, Raritan, NJ, 08869, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(11), 3035-3039
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Three sets of carbapenem-resistant Serratia marcescens isolates have been identified in the United States: 1 isolate in Minnesota in 1985 (before approval of carbapenems for clin. use), 5 isolates in Los Angeles (University of California at Los Angeles [UCLA]) in 1992, and 19 isolates in Boston from 1994 to 1999. All isolates tested produced two .beta.-lactamases, an AmpC-type enzyme with pI values of 8.6 to 9.0 and one with a pI value of approx. 9.5. The enzyme with the higher pI in each strain hydrolyzed carbapenems and was not inhibited by EDTA, similar to the chromosomal class A SME-1 .beta.-lactamase isolated from the 1982 London strain S. marcescens S6. The genes encoding the carbapenem-hydrolyzing enzymes were cloned in Escherichia coli and sequenced. The enzyme from the Minnesota isolate had an amino acid sequence identical to that of SME-1. The isolates from Boston and UCLA produced SME-2, an enzyme with a single amino acid change relative to SME-1, a substitution from valine to glutamine at position 207. Purified SME enzymes from the U.S. isolates had .beta.-lactam hydrolysis profiles similar to that of the London SME-1 enzyme. Pulsed-field gel electrophoresis anal. revealed that the isolates showed some similarity but differed by at least three genetic events. In conclusion, a family of rare class A carbapenem-hydrolyzing .beta.-lactamases first described in London has now been identified in S. marcescens isolates across the United States.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:618672 HCAPLUS
DOCUMENT NUMBER: 133:263637
TITLE: Molecular characterization of FOX-4, a new AmpC-type plasmid-mediated .beta.-lactamase from an Escherichia coli strain isolated in Spain
AUTHOR(S): Bou, German; Oliver, Antonio; Ojeda, Mar; Monzon, Carmelo; Martinez-Beltran, Jesus
CORPORATE SOURCE: Servicio de Microbiologia, Hospital Ramon y Cajal, Madrid, 28034, Spain
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(9), 2549-2553

Search completed by David Schreiber 308-4292

CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A clin. strain of Escherichia coli (Ec GCE) displayed resistance to cefoxitin, cefotetan, cefotaxime, and ceftazidime. Susceptibility was not restored by the addn. of clavulanic acid. Two .beta.-lactamases with apparent pIs of 5.4 and 6.4 were identified; the .beta.-lactamase with a pI of 6.4 was transferred by conjugation and assocd. with a 40-kb plasmid. Anal. of the nucleotide sequence showed a new ampC .beta.-lactamase gene that is closely related to those encoding the FOX-3, FOX-2, and FOX-1 .beta.-lactamases but whose product has four novel amino acid mutations, at positions 11 (M.fwdarw.T), 43 (A.fwdarw.E), 233 (V.fwdarw.A), and 280 (Y.fwdarw.H). This first cephamycinase from Spain was named FOX-4.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:446744 HCAPLUS
DOCUMENT NUMBER: 133:204673
TITLE: Cloning and sequence of the gene encoding a novel cefotaxime-hydrolyzing .beta.-lactamase (CTX-M-9) from Escherichia coli in Spain
AUTHOR(S): Sabate, Montserrat; Tarrago, Raul; Navarro, Ferran; Miro, Elisenda; Verges, Clara; Barbe, Jordi; Prats, Guillermo
CORPORATE SOURCE: Departament de Microbiologia, Hospital de la Santa Creu i Sant Pau, Universitat Autonoma, Barcelona, 08025, Spain
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(7), 1970-1973
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new CTX-M-type .beta.-lactamase (CTX-M-9) has been cloned from a clin. cefotaxime-resistant Escherichia coli strain. Despite the close identity that exists between the CTX-M-9 and Toho-2 .beta.-lactamases (88%), the 35 amino acids located between residues Ala-185 and Ala-219 are totally different in both enzymes. Outside of this region there are only six amino acids substitutions between both proteins.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:446739 HCAPLUS
DOCUMENT NUMBER: 133:190365
TITLE: A novel CTX-M .beta.-lactamase (CTX-M-8) in cefotaxime-resistant Enterobacteriaceae isolated in Brazil
AUTHOR(S): Bonnet, R.; Sampaio, J. L. M.; Labia, R.; De Champs, C.; Sirot, D.; Chanal, C.; Sirot, J.
CORPORATE SOURCE: Laboratoire de Bacteriologie, Faculte de Medecine, Clermont-Ferrand, 63001, Fr.
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(7), 1936-1942
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal

Search completed by David Schreiber 308-4292

LANGUAGE: English

AB To est. the diversity of extended-spectrum .beta.-lactamases in Brazil, 18 strains from different species of the family Enterobacteriaceae exhibiting a pos. double-disk synergy test were collected by a clin. lab. from several hospitals in Rio de Janeiro, Brazil, in 1996 and 1997. Four strains (Proteus mirabilis, Enterobacter cloacae, Enterobacter aerogenes, and Citrobacter amalonaticus) hybridized with a 550-bp CTX-M probe. The P. mirabilis strain produced a CTX-M-2 enzyme. The E. cloacae, E. aerogenes, and C. amalonaticus isolates harbored a bla gene which was identified by cloning and sequencing as a blaCTX-M gene. E. coli HB101 transconjugants and the E. coli DH5.alpha. transformant harboring a recombinant plasmid produced a CTX-M .beta.-lactamase with an isoelec. point of 7.6 conferring a resistance phenotype characterized by a higher level of resistance to cefotaxime than to ceftazidime, as obsd. with the other CTX-M enzymes. The deduced protein sequence showed a novel Ambler class A CTX-M enzyme, named CTX-M-8, which had 83-88% identity with the previously described CTX-M enzymes. The phylogenic study of the CTX-M family including CTX-M-8 revealed 4 CTX-M types, CTX-M-8 being the 1st member of a new phylum of CTX-M enzymes. The evolutionary distances between the 4 types of CTX-M were large, suggesting that the 4 clusters branched off early from a distant unknown enzyme and that intermediate enzymes probably existed.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 60 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:446729 HCAPLUS

DOCUMENT NUMBER: 133:190364

TITLE: Molecular and biochemical heterogeneity of class B carbapenem-hydrolyzing .beta.-lactamases in Chryseobacterium meningosepticum

AUTHOR(S): Bellais, Samuel; Aubert, Daniel; Naas, Thierry; Nordmann, Patrice

CORPORATE SOURCE: Service de Bacteriologie-Virologie, Assistance Publique/Hopitaux de Paris, Faculte de Medecine Paris-Sud, Hopital de Bicetre, Le Kremlin-Bicetre, 94275, Fr.

SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(7), 1878-1886
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Although the carbapenem-hydrolyzing .beta.-lactamase (CH.beta.L) BlaB-1 is known to be in C. meningosepticum NCTC 10585, a 2nd CH.beta.L gene, blaGOB-1, was cloned from another C. meningosepticum clin. isolate (Pt). The G+C content of blaGOB-1 (36%) indicated the likely chromosomal origin of this gene. Its expression in Escherichia coli DH10B yields a mature CH.beta.L with a pI of 8.7 and a relative mol. mass of 28.2 kDa. In E. coli, GOB-1 conferred resistance to narrow-spectrum cephalosporins and reduced susceptibility to ureidopenicillins, broad-spectrum cephalosporins, and carbapenems. GOB-1 had a broad-spectrum hydrolysis profile including penicillins and cephalosporins (but not aztreonam). The catalytic efficiency for meropenem was higher than for imipenem. GOB-1 had low amino acid identity with the class B CH.beta.Ls, sharing 18% with the closest, L-1 from Stenotrophomonas maltophilia, and only 11% with BlaB-1. Most of the conserved amino acids that may be involved in the active site of CH.beta.Ls (His-101, Asp-103, His-162, and His-225) were identified in GOB-1. Sequence heterogeneity was found for GOB-1-like and

BlaB-1-like .beta.-lactamases, having 90 to 100% and 86 to 100% amino acid identity, resp., among 10 unrelated C. meningosepticum isolates. Each isolate had a GOB-1-like and a BlaB-1-like gene. The same combination of GOB-1-like and BlaB-1-like .beta.-lactamases was not found in 2 different isolates. C. meningosepticum is a bacterial species with 2 types of unrelated chromosome-borne class B CH.beta.Ls that can be expressed in E. coli and, thus, may represent a clin. threat if spread in gram-neg. aerobes.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:367595 HCAPLUS
DOCUMENT NUMBER: 133:132213
TITLE: OXA-24, a novel class D .beta.-lactamase with carbapenemase activity in an Acinetobacter baumannii clinical strain
AUTHOR(S): Bou, German; Oliver, Antonio; Martinez-Beltran, Jesus
CORPORATE SOURCE: Servicio de Microbiologia, Hospital Ramon y Cajal, Madrid, 28034, Spain
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(6), 1556-1561
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Acinetobacter baumannii RYC 52763/97, a clin. isolate involved in a prolonged nosocomial outbreak at out hospital, was resistant to all .beta.-lactams tested, including imipenem and meropenem, which had MICs of 128 and 256 .mu.g/mL, resp. This strain synthesized three .beta.-lactamases: a plasmid-mediated TEM-1 .beta.-lactamase (pI 5.4), an AmpC-type chromosomal cephalosporinase (pI 9.4), and a novel, presumptively chromosomally mediated OXA-related enzyme (pI 9.0) named OXA-24. After cloning and sequencing, the deduced amino acid sequence of the OXA-24 .beta.-lactamase showed 40% homol. with the OXA-10 (PSE-2) and OXA-7 .beta.-lactamases, 39% homol. with the OXA-11 and OXA-5 enzymes, and 33% homol. with the LCR-1 .beta.-lactamase. The amino acid sequence of the OXA-24 .beta.-lactamase contained the STFK motif found in serine .beta.-lactamases, but the typical class D triad KTG was replaced by KSG and the motif YGN was replaced by FGN. The OXA-24 .beta.-lactamase hydrolyzed benzylpenicillin and cephaloridine but lacked activity against oxacillin, cloxacillin, and methicillin. The enzymic activity was inhibited by chloride ions and by tazobactam (50% inhibitory concn. [IC50], 0.5 .mu.M), sulbactam (IC50, 40 .mu.M), and clavulanic acid (IC50, 50 .mu.M). Carbapenem MICs for an Escherichia coli transformant (pBMB-1) expressing the cloned OXA-24 enzyme had a fourfold increase. Relative Vmax/Km values of 13 and 6 were obtained with imipenem and meropenem, resp., and a pos. microbiol. assay result with imipenem was obtained with a purified enzymic ext. of this transformant strain. Therefore, we consider this new .beta.-lactamase to be involved in the carbapenem resistance of A. baumannii RYC 52763/97.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:367582 HCAPLUS
DOCUMENT NUMBER: 133:173779
TITLE: Biochemical-genetic characterization and regulation of expression of an ACC-1-like chromosome-borne

cephalosporinase from Hafnia alvei

AUTHOR(S): Girlich, Delphine; Naas, Thierry; Bellais, Samuel; Poirel, Laurent; Karim, Amal; Nordmann, Patrice

CORPORATE SOURCE: Service de Bacteriologie-Virologie, Hopital de Bicetre, Assistance Publique/Hopitaux de Paris, Faculte de Medecine Paris-Sud, Le Kremlin-Bicetre, 94275, Fr.

SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(6), 1470-1478
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A naturally occurring AmpC .beta.-lactamase (cephalosporinase) gene was cloned from the Hafnia alvei 1 clin. isolate and expressed in Escherichia coli. The deduced AmpC .beta.-lactamase (ACC-2) had a pI of 8 and a relative mol. mass of 37 kDa and showed 50 and 47% amino acid identity with the chromosome-encoded AmpCs from Serratia marcescens and Providentia stuartii, resp. It had 94% amino acid identity with the recently described plasmid-borne cephalosporinase ACC-1 from Klebsiella pneumoniae, suggesting the chromosomal origin of ACC-1. The hydrolysis consts. (kcat and Km) showed that ACC-2 was a peculiar cephalosporinase, since it significantly hydrolyzed cefpirome. Once its gene was cloned and expressed in E. coli (pDEL-1), ACC-2 conferred resistance to ceftazidime and cefotaxime but also an uncommon reduced susceptibility to cefpirome. A divergently transcribed ampR gene with an overlapping promoter compared with ampC (blaACC-2) was identified in H. alvei 1, encoding an AmpR protein that shared 64% amino acid identity with the closest AmpR protein from P. stuartii. .beta.-Lactamase induction expts. showed that the ampC gene was repressed in the absence of ampR and was activated when cefoxitin or imipenem was added as an inducer. From H. alvei 1 cultures that expressed an inducible-cephalosporinase phenotype, several ceftazidime- and cefpirome-cross-resistant H. alvei 1 mutants were obtained upon selection on cefpirome- or ceftazidime-contg. plates, and H. alvei 1 DER, a ceftazidime-resistant mutant, stably over-produced cephalosporinase. Transformation of H. alvei 1 DER or E. coli JRG582 (ampDE mutant) harboring ampC and ampR from H. alvei 1 with a recombinant plasmid contg. ampD from E. coli resulted in a decrease in the MIC of .beta.-lactam and recovery of an inducible phenotype for H. alvei 1 DER. Thus, AmpR and AmpD proteins may regulate biosynthesis of the H. alvei cephalosporinase similarly to other enterobacterial cephalosporinases.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 60 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:367578 HCAPLUS

DOCUMENT NUMBER: 133:132211

TITLE: Carbapenemases of Chryseobacterium (Flavobacterium) meningosepticum: Distribution of blaB and characterization of a novel metallo-.beta.-lactamase gene, blaB3, in the type strain, NCTC 10016

AUTHOR(S): Woodford, Neil; Palepou, Marie-France I.; Babini, Gioia S.; Holmes, Barry; Livermore, David M.

CORPORATE SOURCE: Antibiotic Resistance Monitoring and Reference Laboratory, National Collection of Type Cultures, London, NW9 5HT, UK

SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(6), 1448-1452
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Genes encoding carbapenemases in 15 ref. strains of Chryseobacterium (Flavobacterium) meningosepticum from the United Kingdom National Collection of Type Cultures and in one recent clin. isolate were investigated. All the strains hydrolyzed imipenem, but their levels of resistance to carbapenems varied, with imipenem and meropenem MICs ranging from 2 to >32 .mu.g/mL. The blaB gene, which encodes a mol.-class B carbapenemase, was detected in only six ref. strains and in clin. isolate 97/P/5448. The gene from 97/P/5448 had 98% nucleotide identity with the published sequence of blaB (from strain NCTC 10585) and was designated blaB2. A distinct carbapenemase gene, designated blaB3, was cloned from the type strain of C. meningosepticum, NCTC 10016. BlaB3 had an open reading frame of 750 bp with 82% nucleotide identity to blaB and blaB2 and encoded a .beta.-lactamase of 249 amino acids, including the putative signal peptide. This .beta.-lactamase showed 87.6% and 86.7% amino acid homol. with BlaB and BlaB2, resp. BlaB3 was detected in one other ref. strain besides NCTC 10016, but the genetic basis of the carbapenemase activity detected in the other seven ref. strains was not defined. Thus, neither blaB nor blaB3 was ubiquitous in the strains of C. meningosepticum studied, indicating that the ref. strains may represent more than one bacterial species, each with its own intrinsic metallo-.beta.-lactamase. Further taxonomic studies of C. meningosepticum are necessary to resolve this topic. Chryseobacterium spp. are environmental organisms and occasional opportunist pathogens. They apparently represent a reservoir of diverse metallo-.beta.-lactamases, which potentially spread to gram-neg. bacteria of greater clin. significance.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:367576 HCAPLUS
DOCUMENT NUMBER: 133:132342
TITLE: Prevalence of SHV-12 among clinical isolates of Klebsiella pneumoniae producing extended-spectrum .beta.-lactamases and identification of a novel AmpC enzyme (CMY-8) in southern Taiwan
AUTHOR(S): Yan, Jing-Jou; Wu, Shiou-Mei; Tsai, Shu-Huei; Wu, Jiunn-Jong; Su, Ih-Jen
CORPORATE SOURCE: Department of Pathology, National Cheng Kung University Medical Center, National Cheng Kung University Medical College, Tainan, 70101, Taiwan
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(6), 1438-1442
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Twenty (8.5%) of 234 nonrepetitive clin. isolates of Klebsiella pneumoniae from southern Taiwan were found to produce extended-spectrum .beta.-lactamases (ESBLs): 10 strains produced SHV-12, 4 produced SHV-5, 2 produced a non-TEM non-SHV ESBL with a pI of 8.3, 3 produced a novel AmpC .beta.-lactamase designated CMY-8 with a pI of 8.25, and 1 produced SHV-12 and an unidentified AmpC enzyme with a pI of 8.2. The CMY-8 enzyme confers a resistance phenotype similar to CMY-1 and MOX-1, and sequence comparisons showed high homologies (>95%) of nucleotide and amino acid sequences among these three enzymes. Plasmid and pulse-field gel electrophoresis analyses revealed that all isolates harboring an

SHV-derived ESBL were genetically unrelated, indicating that dissemination of resistance plasmids is responsible for the spread of SHV ESBLs among K. pneumoniae in this area. All three isolates carrying CMY-8 had identical genotypic patterns, suggesting the presence of an epidemic strain.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:345154 HCAPLUS
DOCUMENT NUMBER: 133:132337
TITLE: Outbreak of Klebsiella pneumoniae producing transferable AmpC-type .beta.-lactamase (ACC-1) originating from Hafnia alvei
AUTHOR(S): Nadjar, D.; Rouveau, M.; Verdet, C.; Donay, J.-L.; Herrmann, J.-L.; Lagrange, P. H.; Philippon, A.; Arlet, G.
CORPORATE SOURCE: Serv. Bacteriol., Hop. Tenon, Paris, 75970, Fr.
SOURCE: FEMS Microbiology Letters (2000), 187(1), 35-40
CODEN: FMLED7; ISSN: 0378-1097
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Fifty-two strains of Klebsiella pneumoniae producing an AmpC-type plasmid-mediated .beta.-lactamase were isolated from 13 patients in the same intensive care unit between Mar. 1998 and Feb. 1999. These strains were resistant to ceftazidime, cefotaxime and ceftriaxone, but susceptible to cefoxitin, cefepime and aztreonam. Plasmid content and genomic DNA restriction pattern anal. suggested dissemination of a single clone. Two .beta.-lactamases were identified, TEM-1 and ACC-1. We used internal blaACC-1 primers, to sequence PCR products obtained from two unrelated strains of Hafnia alvei. Our results show that the ACC-1 .beta.-lactamase was derived from the chromosome-encoded AmpC-type enzyme of H. alvei.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:217694 HCAPLUS
DOCUMENT NUMBER: 133:1940
TITLE: TLA-1: a new plasmid-mediated extended-spectrum .beta.-lactamase from Escherichia coli
AUTHOR(S): Silva, J.; Aguilar, C.; Ayala, G.; Estrada, M. A.; Garza-Ramos, U.; Lara-Lemus, R.; Ledezma, L.
CORPORATE SOURCE: Departamento de Resistencia Bacteriana, Centro de Investigaciones Sobre Enfermedades Infecciosas, Instituto Nacional de Salud Publica, Morelos, 62508, Mex.
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(4), 997-1003
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Escherichia coli R170, isolated from the urine of an infected patient, was resistant to expanded-spectrum cephalosporins, aztreonam, ciprofloxacin, and ofloxacin but was susceptible to amikacin, cefotetan, and imipenem. This particular strain contained three different plasmids that encoded two .beta.-lactamases with pIs of 7.0 and 9.0. Resistance to cefotaxime, ceftazidime, aztreonam, trimethoprim, and sulfamethoxazole was transferred by conjugation from E. coli R170 to E. coli J53-2. The transferred

plasmid, RZA92, which encoded a single .beta.-lactamase, was 150 kb in length. The cefotaxime resistance gene that encodes the TLA-1 .beta.-lactamase (pI9.0) was cloned from the transconjugant by transformation to E. coli DH5.alpha.. Sequencing of the blaTLA-1 gene revealed an open reading frame of 906 bp, which corresponded to 301 amino acid residues, including motifs common to class A .beta.-lactamases: 70SXXK, 130SDN, and 234KTG. The amino acid sequence of TLA-1 shared 50% identity with the CME-1 chromosomal class A .beta.-lactamase from Chryseobacterium (Flavobacterium) meningosepticum; 48.8% identity with the VEB-1 class A .beta.-lactamase from E. coli; 40 to 42% identity with CblA of Bacteroides uniformis, PER-1 of Pseudomonas aeruginosa, and PER-2 of Salmonella typhimurium; and 39% identity with CepA of Bacteroides fragilis. The partially purified TLA-1 .beta.-lactamase had a mol. mass of 31.4 kDa and a pI of 9.0 and preferentially hydrolyzed cephaloridine, cefotaxime, cephalothin, benzylpenicillin, and ceftazidime. The enzyme was markedly inhibited by sulbactam, tazobactam, and clavulanic acid. TLA-1 is a new extended-spectrum .beta.-lactamase of Ambler class A.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:145278 HCAPLUS
DOCUMENT NUMBER: 132:290903
TITLE: ampR gene mutations that greatly increase class C .beta.-lactamase activity in Enterobacter cloacae
AUTHOR(S): Kuga, Akio; Okamoto, Ryoichi; Inoue, Matsuhisa
CORPORATE SOURCE: Department of Microbiology, Kitasato University School of Medicine, Kanagawa, 228-8555, Japan
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(3), 561-567
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ampC and ampR genes of Enterobacter cloacae GN7471 were cloned into pMW218 to yield pKU403. Four mutant plasmids derived from pKU403 (pKU404, pKU405, pKU406, and pKU407) were isolated in an AmpD mutant of Escherichia coli ML4953 by selection with ceftazidime or aztreonam. The .beta.-lactamase activities expressed by pKU404, pKU405, pKU406, and pKU407 were about 450, 75, 160, and 160 times higher, resp., than that expressed by the original plasmid, pKU403. These mutant plasmids all carried point mutations in the ampR gene. In pKU404 and pKU405, Asp-135 was changed to Asn and Val, resp. In both pKU406 and pKU407, Arg-86 was changed to Cys. The ease of selection of AmpR mutations at a frequency of about 10-6 in this study strongly suggests that derepressed strains, such as AmpD or AmpR mutants, could frequently emerge in the clin. setting.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 15 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:69550 HCAPLUS
DOCUMENT NUMBER: 132:232616
TITLE: Cloning, nucleotide sequencing, and analysis of the gene encoding an AmpC .beta.-lactamase in Acinetobacter baumannii
AUTHOR(S): Bou, German; Martinez-Beltran, Jesus
CORPORATE SOURCE: Servicio de Microbiologia, Hospital Ramon y Cajal, Madrid, 28034, Spain
SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(2),

428-432
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A clin. strain of Acinetobacter baumannii (strain Ab RYC 52763/97) that was isolated during an outbreak in our hospital and that was resistant to all .beta.-lactam antibiotics tested produced three .beta.-lactamases: a TEM-1-type (pI, 5.4) plasmid-mediated .beta.-lactamase, a chromosomally mediated OXA-derived (pI, 9.0) .beta.-lactamase, and a presumptive chromosomal cephalosporinase (pI, 9.4). The nucleotide sequence of the chromosomal cephalosporinase gene shows for the first time the gene encoding an AmpC .beta.-lactamase in A. baumannii. In addn., we report here the biochem. properties of this A. baumannii AmpC .beta.-lactamase.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 16 OF 60 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:11433 HCAPLUS
DOCUMENT NUMBER: 132:163244

TITLE: Genetic-biochemical analysis and distribution of the ambler class A .beta.-lactamase CME-2, responsible for extended-spectrum cephalosporin resistance in Chryseobacterium (Flavobacterium) meningosepticum

AUTHOR(S): Bellais, Samuel; Poirel, Laurent; Naas, Thierry; Girlich, Delphine; Nordmann, Patrice
CORPORATE SOURCE: Service de Bacteriologie-Virologie, Hopital de Bicetre, Assistance Publique/Hopitaux de Paris, Faculte de Medecine Paris-Sud, Le Kremlin-Bicetre, 94275, Fr.

SOURCE: Antimicrobial Agents and Chemotherapy (2000), 44(1), 1-9
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In vitro synergy between extended-spectrum cephalosporins and either clavulanic acid or cefoxitin was found for Chryseobacterium meningosepticum isolates during a double-disk assay on an agar plate. An extended-spectrum .beta.-lactamase (ESBL) gene from a C. meningosepticum clin. isolate was cloned and expressed in Escherichia coli DH10B. Its protein conferred resistance to most .beta.-lactams including extended-spectrum cephalosporins but not to cephamycins or to imipenem. Its activity was strongly inhibited by clavulanic acid, sulbactam, and tazobactam, as well as by cephamycins and imipenem. Sequence anal. of the cloned DNA fragment revealed an open reading frame (ORF) of 891 bp with a G + C content of 33.9%, which lies close to the expected range of G+C contents of members of the Chryseobacterium genus. The ORF encoded a precursor protein of 297 amino acids, giving a mature protein with a mol. mass of 31 kDa and a pI value of 9.2 in E. coli. This gene was very likely chromosomally located. Amino acid sequence comparison showed that this .beta.-lactamase, named CME-2 (C. meningosepticum ESBL), is a novel ESBL of the Ambler class A group (Bush functional group 2be), being weakly related to other class A .beta.-lactamases. It shares only 39 and 35% identities with the ESBLs VEB-1 from E. coli MG-1 and CBL-A from Bacteroides uniformis, resp. The distribution of blaCME-2 among unrelated C. meningosepticum species isolates showed that blaCME-2-like genes were found in the C. meningosepticum strains studied but were absent from strains of other C. meningosepticum-related species. Each C.

meningosepticum strain produced at least two .beta.-lactamases, with one of them being a noninducible serine ESBL with variable pIs ranging from 7.0 to 8.5.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 17 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:585871 HCAPLUS
DOCUMENT NUMBER: 131:319412
TITLE: Cloning of a Chryseobacterium (Flavobacterium) meningosepticum chromosomal gene (blaACME) encoding an extended-spectrum class A .beta.-lactamase related to the Bacteroides cephalosporinases and the VEB-1 and PER .beta.-lactamases
AUTHOR(S): Rossolini, Gian Maria; Franceschini, Nicola; Lauretti, Laura; Caravelli, Berardo; Riccio, Maria Letizia; Galleni, Moreno; Frere, Jean-Marie; Amicosante, Gianfranco
CORPORATE SOURCE: Dipartimento di Biologia Molecolare, Sezione di Microbiologia, Universita degli Studi di Siena, Siena, 53100, Italy
SOURCE: Antimicrobial Agents and Chemotherapy (1999), 43(9), 2193-2199
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In addn. to the BlaB metallo-.beta.-lactamase, Chryseobacterium (Flavobacterium) meningosepticum CCUG 4310 (NCTC 10585) constitutively produces a 31-kDa active-site serine .beta.-lactamase, named CME-1, with an alk. isoelec. pH. The blaACME gene that encodes the latter enzyme was isolated from a genomic library constructed in the Escherichia coli plasmid vector pACYC184 by screening for cefuroxime-resistant clones. Sequence anal. revealed that the CME-1 enzyme is a new class A .beta.-lactamase structurally divergent from the other members of this class, being most closely related to the VEB-1 (also named CEF-1) and PER .beta.-lactamases and the Bacteroides chromosomal cephalosporinases. The blaACME determinant is located on the chromosome and exhibits features typical of those of C. meningosepticum resident genes. The CME-1 protein was purified from an E. coli strain that overexpresses the cloned gene via a T7-based expression system by means of an anion-exchange chromatog. step followed by a gel permeation chromatog. step. Kinetic parameters for several substrates were detd. CME-1 is a clavulanic acid-susceptible extended-spectrum .beta.-lactamase that hydrolyzes most cephalosporins, penicillins, and monobactams but that does not hydrolyze cephamycins and carbapenems. The enzyme exhibits strikingly different kinetic parameters for different classes of .beta.-lactams, with both Km and kcat values much higher for cephalosporins than for penicillins and monobactams. However, the variability of both kinetic parameters resulted in overall similar acylation rates (kcat/Km ratios) for all types of .beta.-lactam substrates.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 18 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:503718 HCAPLUS
DOCUMENT NUMBER: 131:254718
TITLE: A novel type of AmpC .beta.-lactamase, ACC-1, produced by a Klebsiella pneumoniae strain causing nosocomial

pneumonia
AUTHOR(S): Bauernfeind, Adolf; Schneider, Ines; Jungwirth, Renate; Sahly, Hany; Ullmann, Uwe
CORPORATE SOURCE: Max von Pettenkofer Institute, Munich, 80336, Germany
SOURCE: Antimicrobial Agents and Chemotherapy (1999), 43(8), 1924-1931
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A Klebsiella pneumoniae strain resistant to oxyimino cephalosporins was cultured from respiratory secretions of a patient suffering from nosocomial pneumonia in Kiel, Germany, in 1997. The isolate harbors a bla resistance gene located on a transmissible plasmid. An Escherichia coli transconjugant produces a .beta.-lactamase with an isoelec. point of 7.7 and a resistance phenotype characteristic of an AmpC (class 1) .beta.-lactamase except for low MICs of cephamycins. The bla gene was cloned and sequenced. It encodes a protein of 386 amino acids with the active site serine of the S-X-X-K motif at position 64, as is characteristic for class C .beta.-lactamases. Multiple alignment of the deduced amino acid sequence with 21 other AmpC .beta.-lactamases demonstrates only very distant homol., reaching at max. 52.3% identify for the chromosomal AmpC .beta.-lactamase of Serratia marcescens SR50. The .beta.-lactamase of K. pneumoniae KUS represents a new type of AmpC-class enzyme, for which we propose the designation ACC-1 (Ambler class C-1).

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 19 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:483973 HCAPLUS
DOCUMENT NUMBER: 131:238585
TITLE: Molecular characterization of In50, a class 1 integron encoding the gene for the extended-spectrum .beta.-lactamase VEB-1 in Pseudomonas aeruginosa
AUTHOR(S): Naas, Thierry; Poirel, Laurent; Karim, Amal; Nordmann, Patrice
CORPORATE SOURCE: Faculte de Medecine Paris-Sud, Assistance Publique-Hopitaux de Paris, Service de Bacteriologie-Virologie, Hopital de Bicetre, Le Kremlin-Bicetre, 94275, Fr.
SOURCE: FEMS Microbiology Letters (1999), 176(2), 411-419
CODEN: FMLED7; ISSN: 0378-1097
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A clin. isolate of Pseudomonas aeruginosa, JES, was resistant to extended-spectrum cephalosporins with a marked synergistic effect with clavulanic acid on a routine antibiogram. Preliminary PCR anal. revealed the presence of blaVEB-1, an integron-located gene encoding an extended-spectrum .beta.-lactamase previously identified in Escherichia coli MG-1. Using class 1 integron primers and blaVEB-1 intragenic primers, the insert region of the blaVEB-1 contg. integron along with some flanking sequence from P. aeruginosa JES was amplified and subsequently sequenced. In50 contains within its variable region, in addn. to qacE.DELTA.1 and sul1 genes commonly found in class 1 integrons, two gene cassettes, veb1 and aadB. In50 is peculiar since its attI1 site is interrupted by two novel insertion sequences, IS1999 and IS2000. P. aeruginosa JES and Escherichia coli MG-1 strains were isolated from patients previously hospitalized in south east Asian countries. The

finding of blaVEB-1 in these strains and on different integrons underlines the interspecies spread of this integron-located extended-spectrum .beta.-lactamase gene.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 20 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:434750 HCAPLUS
DOCUMENT NUMBER: 131:225406
TITLE: Identification of a novel .beta.-lactamase produced by Xanthomonas campestris, a phytopathogenic bacterium
AUTHOR(S): Weng, Shu-Fen; Chen, Chun-Yi; Lee, Yeong-Sheng; Lin, Juey-Wen; Tseng, Yi-Hsiung
CORPORATE SOURCE: Institute of Molecular Biology, National Chung Hsing University, Taichung, 402, Taiwan
SOURCE: Antimicrobial Agents and Chemotherapy (1999), 43(7), 1792-1797
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Xanthomonas campestris pv. campestris 11 chromosome encodes a periplasmic .beta.-lactamase of 30 kDa. Gene replacement and complementation confirmed the presence of this enzyme. Its deduced amino acid sequence shows identity and conserved domains between it and Stenotrophomonas maltophilia L2 and other Ambler class A/Bush group 2 .beta.-lactamases. Southern hybridization detected a single homologous fragment in each of 12 other Xanthomonas strains, indicating that the presence of a .beta.-lactamase gene is common among xanthomonads.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 21 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:240415 HCAPLUS
DOCUMENT NUMBER: 131:56335
TITLE: Integron-mediated rifampin resistance in Pseudomonas aeruginosa
AUTHOR(S): Tribuddharat, Chanwit; Fennewald, Michael
CORPORATE SOURCE: Department of Microbiology and Immunology, Finch University of the Health Sciences/The Chicago Medical School, North Chicago, IL, 60064, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1999), 43(4), 960-962
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new rifampin resistance gene, arr-2, has been found in Pseudomonas aeruginosa. The ARR-2 protein shows 54% amino acid identity to the rifampin ADP-ribosylating transferase encoded by the arr gene from Mycobacterium smegmatis. This arr-2 gene is located on a gene cassette within a class I integron.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 22 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:159275 HCAPLUS
DOCUMENT NUMBER: 130:334451
TITLE: Molecular and biochemical characterization of VEB-1, a

novel class a extended-spectrum .beta.-lactamase encoded by an Escherichia coli integron gene

AUTHOR(S): Poirel, Laurent; Naas, Thierry; Guibert, Michele; Chaibi, El Bachir; Labia, Roger; Nordmann, Patrice

CORPORATE SOURCE: Service de Bacteriologie-Virologie, Hopital de Bicetre, Faculte de Medecine Paris-Sud, Le Kremlin-Bicetre, 94275, Fr.

SOURCE: Antimicrobial Agents and Chemotherapy (1999), 43(3), 573-581
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A clin. isolate, Escherichia coli MG-1, isolated from a 4-mo-old Vietnamese orphan child, produced a .beta.-lactamase conferring resistance to extended-spectrum cephalosporins and aztreonam. In a disk diffusion test, a typical synergistic effect between ceftazidime or aztreonam and calvulanic acid was obsd. along with an unusual synergy between cefoxitin and cefuroxime. The gene for VEB-1 (Vietnamese extended-spectrum .beta.-lactamase) was cloned and expressed in E. coli JM109. The recombinant plasmid pRLT1 produced a .beta.-lactamase with a pI of 5.35 and conferred high-level resistance to extended-spectrum (or oxyimino) cephalosporins and to aztreonam. Vmax values for extended-spectrum cephalosporins were uncommonly high, while the affinity of the enzyme for ceftazidime and aztreonam was relatively low. BlaVEB-1 showed significant homol. at the DNA level with only blaPER-1 and blaPER-2. Anal. of the deduced protein sequence showed that VEB-1 is a class A penicillinase having very low levels of homol. with any other known .beta.-lactamases. The highest percentage of amino acid identity was 38% with PER-1 or PER-2, two uncommon class A extended-spectrum enzymes. Exploration of the genetic environment of blaVEB-1 revealed the presence of gene cassette features, i.e., (i) a 59-base element assocd. with blaVEB-1; (ii) a second 59-base element just upstream of blaVEB-1, likely belonging to the aacA1-orfG gene cassette; (iii) two core sites (GTTRRRY) on both sides of blaVEB-1; and (i.v.) a second antibiotic resistance gene 3' of blaVEB-1, aadB. blaVEB-1 may therefore be the first class A extended-spectrum .beta.-lactamase that is part of a gene cassette, which itself is likely to be located on a class 1 integron, as sulfamide resistance may indicate. Furthermore, blaVEB-1 is encoded on a large (>100-kb) transferable plasmid found in a Klebsiella pneumoniae MG-2 isolated at the same time from the same patient, indicating a horizontal gene transfer.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 23 OF 60 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:99585 HCAPLUS

DOCUMENT NUMBER: 130:278416

TITLE: Characterization of SFO-1, a plasmid-mediated inducible class A .beta.-lactamase from Enterobacter cloacae

AUTHOR(S): Matsumoto, Yoshimi; Inoue, Matsuhisa

CORPORATE SOURCE: Department of Microbiology, Kitasato University School of Medicine, Sagamihara, Japan

SOURCE: Antimicrobial Agents and Chemotherapy (1999), 43(2), 307-313
CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Enterobacter cloacae 8009 produced an inducible class A .beta.-lactamase which hydrolyzed cefotaxime efficiently. It also hydrolyzed other .beta.-lactams except cephamycins and carbapenems. The activity was inhibited by clavulanic acid and imipenem. The bla gene was transferable to Escherichia coli by electroporation of plasmid DNA. The mol. mass of the .beta.-lactamase was 29 kDa and its pI was 7.3. All of these phenotypic characteristics of the enzyme except for inducible prodn. resemble those of some extended-spectrum class A .beta.-lactamases like FEC-1. The gene encoding this .beta.-lactamase was cloned and sequenced. The deduced amino acid sequence of the .beta.-lactamase was homologous to the AmpA sequences of the Serratia fonticola chromosomal enzyme (96%), MEN-1 (78%), Klebsiella oxytoca chromosomal enzymes (77%), TOHO-1 (75%), and FEC-1 (72%). The conserved sequences of class A .beta.-lactamases, including the S-X(T)-X(S)-K motif, in the active site were all conserved in this enzyme. On the basis of the high degree of homol. to the .beta.-lactamase of S. fonticola, the enzyme was named SFO-1. The ampR gene was located upstream of the ampA gene, and the AmpR sequence of SFO-1 had homol. with the AmpR sequences of the chromosomal .beta.-lactamases from Citrobacter diversus (80%), Proteus vulgaris (68%), and Pseudomonas aeruginosa (60%). SFO-1 was also inducible in E. coli. However, a transformant harboring plasmid without intact ampR produced a small amt. of .beta.-lactamase constitutively, suggesting that AmpR works as an activator of ampA of SFO-1. This is the first report from Japan describing an inducible plasmid-mediated class A .beta.-lactamase in gram-neg. bacteria.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 24 OF 60 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:678206 HCAPLUS

DOCUMENT NUMBER: 130:77771

TITLE: Transferable class C .beta.-lactamases in Escherichia coli strains isolated in Greek hospitals and characterization of two enzyme variants (LAT-3 and LAT-4) closely related to Citrobacter freundii AmpC .beta.-lactamase

AUTHOR(S): Gazouli, M.; Tzouvelekis, L. S.; Vatopoulos, A. C.; Tzelepi, E.

CORPORATE SOURCE: Dep. Bacteriology, Hellenic Pasteur Institute, Athens, 11521, Greece

SOURCE: Journal of Antimicrobial Chemotherapy (1998), 42(4), 419-425
CODEN: JACHDX; ISSN: 0305-7453

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Among 2133 isolates of Escherichia coli obtained during 1996 from 10 Greek hospitals, 63 (3%) were resistant to cefoxitin. Typing by ERIC2-PCR indicated that the cefoxitin-resistant (FOXr) isolates were distinct. .beta.-Lactamase studies and hybridization expts. showed that most strains produced .beta.-lactamases related to the AmpC chromosomal cephalosporinase of Citrobacter freundii. The enzymes were encoded by similar non-self-transmissible plasmids. The bla genes encoding two .beta.-lactamases (LAT-3 and LAT-4) with isoelec. points 8.9 and 9.4, resp., were cloned and sequenced. The deduced amino acid sequences displayed a high degree of homol. (>95%) with the AmpC .beta.-lactamase of C. freundii. The patterns of resistance to .beta.-lactams of the FOXr E. coli depended on the quantity of class C enzymes and the simultaneous expression of other .beta.-lactamases. In a few isolates a 36 kDa

outer-membrane protein, presumably a porin, was not expressed at detectable quantities. These isolates were resistant to cefoxitin, and their susceptibility to the other .beta.-lactams tested was not significantly decreased.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 25 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:580631 HCAPLUS
DOCUMENT NUMBER: 129:299507
TITLE: Two novel plasmid-mediated cefotaxime-hydrolyzing .beta.-lactamases (CTX-m-5 and CTX-m-6) from Salmonella typhimurium
AUTHOR(S): Gazouli, Maria; Tzelepi, Eva; Markogiannakis, Antonios; Legakis, Nicholas J.; Tzouvelekis, Leonidas S.
CORPORATE SOURCE: Dep. Bacterology, Hellenic Pasteur Institute, Athens, 11521, Greece
SOURCE: FEMS Microbiology Letters (1998), 165(2), 289-293
CODEN: FMLED7; ISSN: 0378-1097
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two novel plasmid-mediated .beta.-lactamases (CTX-M-5 and CTX-M-6) produced by Salmonella typhimurium clin. strains were characterized. The enzymes exhibited a pI of 8.4, hydrolyzed oxyimino-.beta.-lactams and were susceptible to mechanism-based .beta.-lactamase inhibitors. The resp. bla genes were cloned and sequenced. The deduced amino acid sequences showed a high degree of homol. with those of the previously described plasmid class A CTX-M-type enzymes and appeared related to the chromosomal .beta.-lactamases of Klebsiella oxytoca.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 26 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:516808 HCAPLUS
DOCUMENT NUMBER: 129:241602
TITLE: CTX-M-5, a novel cefotaxime-hydrolyzing .beta.-lactamase from an outbreak of Salmonella typhimurium in Latvia
AUTHOR(S): Bradford, Patricia A.; Yang, Youjun; Sahm, Daniel; Grope, Ilze; Gardovska, Dace; Storch, Gregory
CORPORATE SOURCE: Wyeth-Ayerst Research, Pearl River, NY, 10965, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(8), 1980-1984
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB At a children's hospital in Riga, Latvia, isolates identified as Salmonella typhimurium were found to be resistant to expanded-spectrum cephalosporins. Two of the resistant strains were analyzed for the mechanism of cephalosporin resistance. Isoelec. focusing revealed a common .beta.-lactamase with a pI of 8.8. In addn., one of the strains produced a pI 7.6 .beta.-lactamase. A transconjugant producing only the pI 7.6 enzyme was susceptible to expanded-spectrum cephalosporins: therefore, this enzyme was most likely SHV-1. Transformants producing only the pI 8.8 .beta.-lactamase were resistant to cefotaxime and aztreonam but were susceptible or intermediate to ceftazidime. A

substrate profile detd. spectrophotometrically with purified enzyme revealed potent activity against cefotaxime, with a relative kcat value of 95 (benzylpenicillin equal to 100). The enzyme showed lower relative kcat values for ceftazidime (3.3) and aztreonam (9.3). In addn., the enzyme was inhibited by clavulanate, sulbactam and tazobactam, with 50% inhibitory concns. of 19, 100, and 3.4 nM, resp. These results indicated the presence of an unusual extended-spectrum .beta.-lactamase. The gene expressing the pI 8.8 .beta.-lactamase was cloned. Nucleotide sequencing revealed a .beta.-lactamase gene that differs from the gene encoding CTX-M-2, which also originated from S. typhimurium, by 11 nucleotides, 4 of which result in amino acid substitutions:Ala27Thr, Val230Gly, Glu254Ala, and Ile278Val. These results indicated the presence of a novel extended-spectrum .beta.-lactamase, designated CTX-M-5, that specifically confers resistance to cefotaxime.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 27 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:516806 HCAPLUS
DOCUMENT NUMBER: 129:227442
TITLE: Structure of CARB-4 and AER-1 carbenicillin-hydrolyzing .beta.-lactamases
AUTHOR(S): Sanschagrin, Francois; Bejaoui, Noureddine; Levesque, Roger C.
CORPORATE SOURCE: Microbiologie Moleculaire et Genie des Proteines, Sciences de la Vie et de la Sante, Faculte de Medecine et Pavillon Charles-Eugene Marchand, Universite Laval, Ste-Foy, QC, G1K 7P4, Can.
SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(8), 1966-1972
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The nucleotide sequences of blaCARB-4 encoding CARB-4 was detd. and a polypeptide of 288 amino acids deduced. The gene was characterized as a variant of group 2c carbenicillin-hydrolyzing .beta.-lactamases such as PSE-4, PSE-1, and CARB-3. The level of DNA homol. between the bla genes for these .beta.-lactamases varied from 98.7 to 99.9%, while that between these genes and blaCARB-4 encoding CARB-4 was 86.3%. The blaCARB-4 gene was acquired from some other source because it has a G+C content of 39.1%, compared to a G+C content of 67% for typical Pseudomonas aeruginosa genes. DNA sequencing revealed that blaAER-1 shared 60.8% DNA identity with blaPSE-3 encoding PSE-3. The deduced AER-1 .beta.-lactamase peptide was compared to class A, B, C, and D enzymes and had 57.6% identity wit PSE-3, including an STHK tetrad at the active site. For CARB-4 and AER-1, conserved canonical amino acid boxes typical of class A .beta.-lactamases were identified in a multiple alignment. Anal. of the DNA sequences flanking blaCARB-4 and blaAER-1 confirmed the importance of gene cassettes acquired via integrons in bla gene distribution.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 28 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:370363 HCAPLUS
DOCUMENT NUMBER: 129:119537
TITLE: Characterization and sequence of the Chryseobacterium (Flavobacterium) meningosepticum carbapenemase: a new molecular class B .beta.-lactamase showing a broad

substrate profile
AUTHOR(S): Rossolini, Gian Maria; Franceschini, Nicola; Riccio, Maria Letizia; Mercuri, Paola Sandra; Perilli, Mariagrazia; Galleni, Moreno; Frere, Jean-Marie; Amicosante, Gianfranco
CORPORATE SOURCE: Dipartimento di Biologia Molecolare, Sezione di Microbiologia, Universita di Siena, Siena, 53100, Italy
SOURCE: Biochemical Journal (1998), 332(1), 145-152
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The metallo-.beta.-lactamase produced by Chryseobacterium (formerly Flavobacterium) meningosepticum, which is the flavobacterial species of greatest clin. relevance, was purified and characterized. The enzyme, named BlaB, contains a polypeptide with an apparent Mr of 26,000, and has a pI of 8.5. It hydrolyzes penicillins, cephalosporins (including cefoxitin), carbapenems and 6-.beta.-iodopenicillanate, a mechanism-based inactivator of active-site serine .beta.-lactamases. The enzyme was inhibited by EDTA, 1-10 phenanthroline and pyridine-2,6-dicarboxylic acid, with different inactivation parameters for each chelating agent. The C. meningosepticum blaB gene was cloned and sequenced. According to the G + C content and codon usage, the blaB gene appeared to be endogenous to the species. The BlaB enzyme showed significant sequence similarity to other class B .beta.-lactamases, being overall more similar to members of subclass B1, which includes the metallo-enzymes of Bacillus cereus (Bc-II) and Bacteroides fragilis (CcrA) and the IMP-1 enzyme found in various microbial species, and more distantly related to the metallo-.beta.-lactamases of Aeromonas spp. (CphA, CphA2 and ImiS) and of Stenotrophomonas maltophilia (L1).
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 29 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:271698 HCAPLUS
DOCUMENT NUMBER: 129:63798
TITLE: Sequence of the gene encoding a plasmid-mediated cefotaxime-hydrolyzing glass A .beta.-lactamase (CTX-M-4): involvement of serine 237 in cephalosporin hydrolysis
AUTHOR(S): Gazouli, Maria; Tzelepi, Eva; Sidorenko, Sergei V.; Tzouvelekis, Leonidas S.
CORPORATE SOURCE: Department of Bacteriology, Hellenic Pasteur Institute, Athens, 11521, Greece
SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(5), 1259-1262
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The sequence of the gene encoding a novel cefotaxime-hydrolyzing .beta.-lactamase (CTX-M-4) was detd. It was located in a plasmid harbored by a Salmonella typhimurium strain. CTX-M-4 was similar to the plasmidic cefotaxime-hydrolyzing .beta.-lactamases CTX-M-2 and Toho-1 and related to the chromosomal .beta.-lactamase of Klebsiella oxytoca. A Ser-237.fwdarw.Ala substitution, introduced by site-directed mutagenesis, caused minor alterations in the interaction of CTX-M-4 with .beta.-lactams, reducing slightly the relative hydrolytic activity against

cefotaxime and the susceptibility to inhibition by clavulanate.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 30 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:255535 HCAPLUS
DOCUMENT NUMBER: 129:37900
TITLE: Cefotaxime-resistant Enterobacteriaceae isolates from a hospital in Warsaw, Poland: identification of a new CTX-M-3 cefotaxime-hydrolyzing .beta.-lactamase that is closely related to the CTX-M-1/MEN-1 enzyme
AUTHOR(S): Gniadkowski, Marek; Schneider, Ines; Palucha, Andrzej; Jungwirth, Renate; Mikiewicz, Barbara; Bauernfeind, Adolf
CORPORATE SOURCE: Seru and Vaccines Central Research Laboratory, Warsaw, 00-725, Pol.
SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(4), 827-832
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A group of cefotaxime-resistant Citrobacter freundii and Escherichia coli isolates were collected by a clin. lab. in a hospital in Warsaw, Poland, in July 1996. Detailed anal. has shown that all of these produced a .beta.-lactamase (pI, 8.4) belonging to the CTX-M family, one of the minor extended-spectrum .beta.-lactamase families with a strong cefotaxime-hydrolyzing activity. Sequencing has revealed that C. freundii isolates produced a new CTX-M-3 enzyme which is very closely related to the CTX-M-1/MEN-1 .beta.-lactamase, sporadically identified in Europe over a period of 6 yr. Amino acid sequences of these two .beta.-lactamases differ at four positions: Val77Ala, Asp114Asn, Ser140Ala, and Asn288Asp (the first amino acid of each pair refers to CTX-M-1/MEN-1 and second refers to CTX-M-3). The partial sequence of the E. coli CTX-M gene was identical to the corresponding region of blaCTX-M-3, but a transconjugant of the E. coli isolate expressed higher levels of resistance to .beta.-lactams than did C. freundii transconjugants. These resistance differences correlated with differences in plasmid DNA restriction patterns. Our results suggest that CTX-M genes have been spread among different species of the family Enterobacteriaceae in the hospital and that the CTX-M-3-expressing C. freundii strain causing routine urinary tract infections has been maintained for a relatively long time in the hospital environment.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 31 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:75626 HCAPLUS
DOCUMENT NUMBER: 128:280025
TITLE: Characterization of FOX-3, an AmpC-type plasmid-mediated .beta.-lactamase from an Italian isolate of Klebsiella oxytoca
AUTHOR(S): Marchese, Anna; Arlet, Guillaume; Schito, Gian Carlo; Lagrange, Philippe H.; Philippon, Alain
CORPORATE SOURCE: Istituto Di Microbiologia, Genoa, 16132, Italy
SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(2), 464-467
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology

Search completed by David Schreiber 308-4292

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Klebsiella oxytoca 1731, which showed a wide spectrum of resistance to .beta.-lactams, including cefoxitin, was isolated in 1994 from a patient in Genoa, Italy. This strain contained a plasmid-mediated AmpC .beta.-lactamase with a pI of 7.25. Sequencing of the corresponding DNA of K. oxytoca 1731 revealed 96 and 97% identities of the deduced amino acid sequence with FOX-1 and FOX-2, resp.

L11 ANSWER 32 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:24778 HCAPLUS
DOCUMENT NUMBER: 128:202250
TITLE: Sequences of homologous .beta.-lactamases from clinical isolates of Serratia marcescens with different substrate specificities
AUTHOR(S): Matsumura, Naoki; Minami, Shinzaburo; Mitsuhashi, Susumu
CORPORATE SOURCE: Episome Institute, Gunma, Japan
SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(1), 176-179
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Genes for two group 1 .beta.-lactamases, SRT-1 and SST-1, were sequenced. These .beta.-lactamases were produced by clin. isolates of Serratia marcescens, isolates GN16694 and GN19450, resp. The resulting enzymes were 96% identical. SRT-1 hydrolyzed oxyimino cephalosporins, but SST-1 hardly hydrolyzed them. At residue 213 in the third motif, which is conserved among group 1 .beta.-lactamases, SRT-1 and SST-1 had Lys and Glu, resp. By site-directed mutagenesis, the substitution of Glu by Lys at residue 213 in SST-1 resulted in an enzyme that hydrolyzed oxyimino cephalosporins.

L11 ANSWER 33 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:597400 HCAPLUS
DOCUMENT NUMBER: 127:316583
TITLE: A novel class C .beta.-lactamase (FOX-2) in Escherichia coli conferring resistance to cephamycins
AUTHOR(S): Bauernfeind, A.; Wagner, S.; Jungwirth, R.; Schneider, I.; Meyer, D.
CORPORATE SOURCE: Max von Pettenkofer-Institut, Munich, 80336, Germany
SOURCE: Antimicrobial Agents and Chemotherapy (1997), 41(9), 2041-2046
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An E. coli strain resistant to a broad spectrum of .beta.-lactams, including cephamycins, was isolated from a patient suffering from urinary tract infection. A resistance plasmid (pMVP-7) was transferred from the clin. isolate to an E. coli recipient. Both strains produce a cefoxitin-hydrolyzing .beta.-lactamase focusing at pI 6.7. The phenotype was similar to that of a Klebsiella pneumoniae strain producing cephamycinase FOX-1, so primers were selected from the FOX-1 sequence to amplify the bla gene of the transconjugant. The PCR product obtained was sequenced. The percentage of identity of the deduced amino acid sequence with sequences of other AmpC-type .beta.-lactamases was 96.9% with FOX-1, 74.9% with CMY-1, and 67.7% with MOX-1. This new plasmid-mediated enzyme

is most closely related to FOX-1 (11 amino acid exchanges). The designation FOX-2 is therefore proposed.

L11 ANSWER 34 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:469259 HCAPLUS
DOCUMENT NUMBER: 127:230992
TITLE: Characterization and amino acid sequence analysis of a new oxyimino cephalosporin-hydrolyzing class A .beta.-lactamase from Serratia fonticola CUV
AUTHOR(S): Peduzzi, Jean; Farzaneh, Sedigheh; Reynaud, Alain; Barthelemy, Michel; Labia, Roger
CORPORATE SOURCE: Museum National Histoire Naturelle, CNRS URA 401, IFR 63, 63, Rue Buffon, Paris, 75231/5, Fr.
SOURCE: Biochimica et Biophysica Acta (1997), 1341(1), 58-70
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Serratia fonticola CUV produces 2 isoenzymes (forms I and II) with .beta.-lactamase activity which were purified by a 5-step procedure. The isoenzymes had identical kinetic parameters and isoelec. point (pI = 8.12). They were characterized by a specific activity towards benzylpenicillin of 1650 U/mg. The .beta.-lactamase hydrolyzed benzylpenicillin, amoxycillin, ureidopenicillins, first- and second-generation cephalosporins. Carboxypenicillins and isoxazolylpenicillins were hydrolyzed to a lesser extent. Towards cefotaxime and ceftriaxone (third-generation cephalosporins), the S. fonticola enzyme exhibited catalytic efficiencies much higher than those of MEN-1 and extended-spectrum TEM deriv. .beta.-lactamases. The .beta.-lactamase from S. fonticola was markedly inhibited by .beta.-lactamase inhibitors such as clavulanic acid, sulbactam and tazobactam. The purified isoenzymes were digested by trypsin, endoproteinase Asp-N, and chymotrypsin. Amino acid sequence detns. of the resulting peptides allowed the alignment of 267 amino acid residues (Swiss-Prot, accession no. P 80545) for form I .beta.-lactamase. Form II is 5 residues shorter than form I at its N-terminus. From amino acid sequence comparisons, S. fonticola CUV .beta.-lactamase was found to share >69.3% identity with the chromosomally encoded .beta.-lactamases of Klebsiella oxytoca, Proteus vulgaris, Citrobacter diversus, and the plasmid-mediated enzymes MEN-1 and Toho-1. Therefore, the oxyimino cephalosporin-hydrolyzing .beta.-lactamase of S. fonticola belongs to Ambler's class A. Contribution of the serine at ABL 237 in the broad-spectrum activity of these .beta.-lactamases is discussed.

L11 ANSWER 35 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:438878 HCAPLUS
DOCUMENT NUMBER: 127:172966
TITLE: Sequence analysis and enzyme kinetics of the L2 serine .beta.-lactamase from Stenotrophomonas maltophilia
AUTHOR(S): Walsh, T. R.; Macgowan, A. P.; Bennett, P. M.
CORPORATE SOURCE: Bristol Centre for Antimicrobial Research and Evaluation (BCARE), Department of Microbiology and Pathology, Medical School, University of Bristol, Bristol, BS8 1TD, UK
SOURCE: Antimicrobial Agents and Chemotherapy (1997), 41(7), 1460-1464
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal

Search completed by David Schreiber 308-4292

LANGUAGE: English

AB The L2 serine active-site .beta.-lactamase from Stenotrophomonas maltophilia has been classified as a clavulanic acid-sensitive cephalosporinase. The gene encoding this enzyme from S. maltophilia 1275 IID has been cloned on a 3.3-kb fragment into pK18 under the control of a Ptac promoter to generate recombinant plasmid pUB5840; when expressed in Escherichia coli, this gene confers resistance to cephalosporins and penicillins. Sequence anal. has revealed an open reading frame (ORF) of 909 bp with a GC content of 71.6%, comparable to that of the L1 metallo-.beta.-lactamase gene (68.4%) from the same bacterium. The ORF encodes an unmodified protein of 303 amino acids with a predicted mol. mass of 31.5 kDa, accommodating a putative leader peptide of 27 amino acids. Comparison of the amino acid sequence with those of other .beta.-lactamases showed it to be most closely related (54% identity) to the BLA-A .beta.-lactamase from Yersinia enterocolitica. Sequence identity is most obvious near the STXK active-site motif and the SDN loop motif common to all serine active-site penicillinases. Sequences outside the conserved regions display low homol. with comparable regions of other class A penicillinases. Kinetics of the enzyme from the cloned gene demonstrated an increase in activity with cefotaxime but markedly less activity with imipenem than previously reported. Hence, the S. maltophilia L2 .beta.-lactamase is an inducible Ambler class A .beta.-lactamase which would account for the sensitivity to clavulanic acid.

L11 ANSWER 36 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:544240 HCAPLUS
DOCUMENT NUMBER: 125:215345
TITLE: Characterization of IMI-1 .beta.-lactamase, a class A carbapenem-hydrolyzing enzyme from Enterobacter cloacae
AUTHOR(S): Rasmussen, Beth A.; Bush, Karen; Keeney, David; Yang, Youjun; Hare, Roberta; O'Gara, Clotilde; Medeiros, Antone A.
CORPORATE SOURCE: Wyeth Ayerst Research, Lederle Laboratories, Pearl River, NY, 10965, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1996), 40(9), 2080-2086
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In 1984, a year prior to the U.S. approval of imipenem for clin. use, a wound isolate and a bile isolate of Enterobacter cloacae were obtained from two patients in a California hospital. These isolates were resistant to imipenem, penicillins, and inhibitor combinations; early cephalosporins such as cephalothin, cefamandole, and cefoxitin; and cefoperazone. However, they were susceptible (MICs <4 .mu.g/mL) to cefotaxime, ceftriaxone, ceftazidime, and moxalactam. Both strains produced an apparent TEM-1 .beta.-lactamase; an inducible NmcA-type imipenem-hydrolyzing .beta.-lactamase, IMI-1, with a pI of 7.05; and an inducible .beta.-lactamase with a pI of 8.1, typical of an E. cloacae AmpC .beta.-lactamase. Purified IMI-1 hydrolyzed imipenem and benzylpenicillin at modest rates, but more slowly than cephaloridine. The enzyme was inhibited by clavulanic acid and tazobactam. EDTA did not inhibit the cephaloridine-hydrolyzing activity. The .beta.-lactamase gene encoding IMI-1, imiA1, was cloned from E. cloacae 1413B. Sequence anal. identified the imiA1 gene as encoding a class A serine .beta.-lactamase. Both the imiA1 DNA and encoded amino acid sequences shared greater than 95%

identity with the NmcA gene and its encoded protein. DNA sequence anal. also identified a gene upstream of imiA1 that shares >95% identity with nmcR and that may encode a regulatory protein. In conclusion, IMI-1, a carbapenem-hydrolyzing .beta.-lactamase inhibited by clavulanic acid, was identified as a group 2f, class A, carbapenem-hydrolyzing cephalosporinase.

L11 ANSWER 37 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:469992 HCAPLUS
DOCUMENT NUMBER: 125:161989
TITLE: Comparative characterization of the cephamycinase blaCMY-1 gene and its relationship with other .beta.-lactamase genes
AUTHOR(S): Bauernfeind, A.; Stemplinger, I.; Jungwirth, R.; Wilhelm, R.; Chong, Y.
CORPORATE SOURCE: Max von Pettenkofer-Institut, Munich, Germany
SOURCE: Antimicrobial Agents and Chemotherapy (1996), 40(8), 1926-1930
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A plasmidic .beta.-lactamase which hydrolyzes cephamycins was first detected and reported in 1989. At that time its description was restricted to phenotypic characteristics. We analyzed the nucleotide sequence of its gene and explored its genetic relationship with other bla genes. The deduced amino acid sequence of the blaCMY-1 product was compared with those of other known plasmidic cephamycinases and of chromosomal AmpC .beta.-lactamases. The results indicate that the relationship of CMY-1 is closest to MOX-1 among the plasmidic cephamycinases and to AmpC of Pseudomonas aeruginosa among the chromosomal cephalosporinases. We conclude that the plasmidic cephamycinases described up to now may be classified into three families, as follows: CMY-1, MOX-1, and FOX-1 with AmpC of P. aeruginosa; CMY-2, BIl-1, and LAT-1 with AmpC of Citrobacter freundii; and MIR-1 with AmpC of Enterobacter cloacae. Plasmidic cephamycinases are now recognized as clin. relevant class C .beta.-lactamases.

L11 ANSWER 38 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:355040 HCAPLUS
DOCUMENT NUMBER: 125:78447
TITLE: A gene product related to TraI is required for the mobilization of Bacteroides mobilizable transposons and plasmids
AUTHOR(S): Smith, C. Jefrry; Parker, Anita C.
CORPORATE SOURCE: Dep. Microbiology Immunology, East Carolina Univ. Sch. Medicine, Greenville, NC, 27848-4354, USA
SOURCE: Molecular Microbiology (1996), 20(4), 741-750
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antibiotic-resistance transposon Tn4555 from Bacteroids can be transferred between strains by conjugation. The transposon is not self-transmissible and must be mobilized by resident chromosomal tetracycline-resistance elements. In the present report, the mechanism of transfer was examd. at the genetic level by deletion anal. and nucleotide sequencing of clones that conferred a transmissible phenotype on a non-mobilizable plasmid. The results suggested that the product of mobATn

was required for mobilization and it worked in concert with a cis-acting oriT-like sequence. This mechanism was compared with the mobilization system of a cryptic Bacteroides plasmid, pBI143, and the two systems were found to share a common transfer strategy. The mobA gene products from both genetic elements were related and they had limited homol. to the broad group of mobilization proteins (relaxases) typified by TraI of RP4. Phylogenetic anal. of MobA and several other mobilization proteins from commensal gastrointestinal tract organisms suggested that they formed a new subgroup of the TraI superfamily. The mobilization regions of both Tn4555 and pBI143 were located on discrete segments of DNA within the the parent genetic element. These segments were delineated by regions of secondary structure, suggesting that they could be defined mobilization cassettes.

L11 ANSWER 39 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:207023 HCAPLUS
DOCUMENT NUMBER: 124:334511
TITLE: Molecular analysis of the gene cluster involved in cephalosporin biosynthesis from Lysobacter lactamgenus YK90
AUTHOR(S): Kimura, H.; Izawa, M.; Sumino, Y.
CORPORATE SOURCE: Fermentation Center, Takeda Chemical Industries Ltd., Osaka, 532, Japan
SOURCE: Applied Microbiology and Biotechnology (1996), 44(5), 589-96
CODEN: AMBIDG; ISSN: 0175-7598
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Detn. of the nucleotide sequence downstream from the Lysobacter lactamgenus pcbC gene encoding isopenicillin N synthase revealed that 5 open-reading frames (ORF) including the pcbC gene were tightly linked in the same orientation. Each ORF has the remarkable feature of the protein-coding frame in the DNA sequence with a high G + C content. Expression in Escherichia coli and a comparison of the deduced amino acid sequences with published sequences showed that the gene cluster contained a deacetoxycephalosporin C synthetase (DAOCS) gene (cefE), an ORF having homol. with the Cephalosporium acremonium DAOCS/deacetylcephalosporin C synthetase gene (cefEF), an isopenicillin N epimerase gene(cefD), and a .beta.-lactamase gene. The gene order was pcbC-cefE-ORF3-cefD-.beta.-lactamase.

L11 ANSWER 40 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:86193 HCAPLUS
DOCUMENT NUMBER: 124:280519
TITLE: Sequences of .beta.-lactamase genes encoding CTX-M-1 (MEN-1) and CTX-M-2 and relationship of their amino acid sequences with those of other .beta.-lactamases
AUTHOR(S): Bauernfeind, A.; Stemplinger, I.; Jungwirth, R.; Ernst, S.; Casellas, J. M.
CORPORATE SOURCE: Max von Pettenkofer-Inst., Punta Chica, Argent.
SOURCE: Antimicrobial Agents and Chemotherapy (1996), 40(2), 509-13
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Amino acid sequences detd. either by protein sequencing or by protein sequencing are identical for cefotaximases CTX-M-1 and MEN-1, whereas

CTX-M-2 is 84% identical to CTX-M-1/MEN-1. Both .beta.-lactamases are distantly related to other plasmidic class A enzymes (homol. to TEM-1 is 38.1% for CTX-M-1/Men-1 and 36.5% for CTX-M-2); the closest relationship was with the chromosomal .beta.-lactamase of Klebsiella oxytoca E23004 (homols. of 74.5% for CTX-M-1/MEN-1 and 77.9% for CTX-M2). The cefotaximases CTX-M-1/MEN-1 and CTX-M-2 represent two members of a new subgroup of plasmidic class A .beta.-lactamases.

L11 ANSWER 41 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:837305 HCAPLUS
DOCUMENT NUMBER: 124:3848
TITLE: Cloning and sequence of the gene encoding a cefotaxime-hydrolyzing class A .beta.-lactamase isolated from Escherichia coli
AUTHOR(S): Ishii, Yoshikazu; Ohno, Akira; Taguchi, Hayao; Imajo, Seiichi; Ishiguro, Masaji; Matsuzawa, Hiroshi
CORPORATE SOURCE: Dep. Microbiology, Toho Univ. Sch. Med., Tokyo, 143, Japan
SOURCE: Antimicrobial Agents and Chemotherapy (1995), 39(10), 2269-75
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Escherichia coli TUH12191, which is resistant to piperacillin, cefazolin, cefotiam, ceftizoxime, cefuzonam, and aztreonam but is susceptible to cefoxitin, latamoxef, flomoxef, and imipenem, was isolated from the urine of a patient treated with .beta.-lactam antibiotics. The .beta.-lactamase (Toho-1) purified from the bacteria had a pI of 7.8, had a mol. wt. of about 29,000, and hydrolyzed .beta.-lactam antibiotics such as penicillin G, ampicillin, oxacillin, carbenicillin, piperacillin, cephalothin, cephaloridine, cefoxitin, cefotaxime, ceftazidime, and aztreonam. Toho-1 was markedly inhibited by .beta.-lactamase inhibitors such as clavulanic acid and tazobactam. Resistance to .beta.-lactams, streptomycin, spectinomycin, sulfamethoxazole, and trimethoprim was transferred by conjugational transfer from E. coli TUH12191 to E. coli ML4903, and the transferred plasmid was about 58 kbp, belonging to incompatibility group M. The cefotaxime resistance gene for Toho-1 was subcloned from the 58-kbp plasmid by transformation of E. coli MV1184. The sequence of the gene for Toho-1 was detd., and the open reading frame of the gene consisted of 873 or 876 bases (initial sequence, ATGATG). The nucleotide sequence of the gene (DDBJ accession no. D37830) was found to be about 73% homologous to the sequence of the gene encoding a class A .beta.-lactamase produced by Klebsiella oxytoca E23004. According to the amino acid sequence deduced from the DNA sequence, the precursor consisted of 290 or 291 amino acid residues, which contained amino acid motifs common to class A .beta.-lactamases (70SXXK, 130SDN, and 234KTG). Toho-1 was about 83% homologous to the .beta.-lactamase mediated by the chromosome of K. oxytoca D488 and the .beta.-lactamase mediated by the plasmid of E. coli MEn-1. Therefore, the newly isolated .beta.-lactamase Toho-1 produced by E. coli TUH12191 is similar to .beta.-lactamases produced by K. oxytoca D488, K. oxytoca E23004, and E. coli MEN-1 rather than to mutants of TEM or SHV enzymes. Toho-1 has shown the highest degree of similarity to K. oxytoca class A .beta.-lactamase. Detailed comparison of Toho-1 with other .beta.-lactamases implied that replacement of Asn-276 by Arg with the concomitant substitution of Thr for Arg-244 is an important mutation in the extension of the substrate specificity.

L11 ANSWER 42 OF 60 HCAPLUS COPYRIGHT 2003 ACS

Search completed by David Schreiber 308-4292

ACCESSION NUMBER: 1995:793578 HCAPLUS
DOCUMENT NUMBER: 124:2003
TITLE: Sequence analysis of two chromosomally mediated inducible .beta.-lactamases from Aeromonas sobria, strain 163a, one a class D penicillinase, the other an AmpC cephalosporinase
AUTHOR(S): Walsh, Timothy R.; Hall, Len; MacGowan, Alasdair P.; Bennett, Peter M.
CORPORATE SOURCE: School Medical Sciences, Univ. Bristol, Bristol, BS8 1TD, UK
SOURCE: Journal of Antimicrobial Chemotherapy (1995), 36(1), 41-52
CODEN: JACHDX; ISSN: 0305-7453
PUBLISHER: Saunders
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two .beta.-lactamase genes from Aeromonas sobria, strain 163a, have been cloned and sequenced, one encoding a typical class C cephalosporinase, designated CepS, the other a class D penicillinase, designated AmpS. CepS is predicted to be a mature protein of 38 kDa with a pI value of 7.0. The amino acid sequence of CepS is most similar to that of AmpC from Pseudomonas aeruginosa (54.7%). AmpS is predicted to be a mature protein of 27 kDa with a pI value of 7.9 that most closely resembles BLAD from Klebsiella pneumoniae (42.2%), and OXA-1 from Escherichia coli (36.6%), .beta.-lactamases that are encoded by genes carried on multi-resistant transposons. AmpS differs significantly from the other class D .beta.-lactamases in that it hydrolyses cloxacillin poorly and is inducible. Both genes exhibit a high overall GC content and possess a high NNC and NNG codon preference, similar to that of genes from Pseudomonas spp.

L11 ANSWER 43 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:789086 HCAPLUS
DOCUMENT NUMBER: 123:331496
TITLE: Cloning and expression of the isopenicillin N synthase gene from Lysobacter lactamgenus YK90
AUTHOR(S): Kimura, Hiroyuki; Suzuki, Masaru; Sumino, Yasuhiro
CORPORATE SOURCE: Fermentation Center, Takeka Chemical Industries, Ltd., Osaka, 532, Japan
SOURCE: Journal of Fermentation and Bioengineering (1995), 80(2), 118-23
CODEN: JFBIEX; ISSN: 0922-338X
PUBLISHER: Society for Fermentation and Bioengineering, Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Lysobacter lactamgenus YK90 pcbC gene encoding isopenicillin N synthase (IPNS) was cloned using the corresponding Acremonium chrysogenum pcbC gene as a probe. The cloned pcbC gene encoded a polypeptide composed of 326 amino acid residues with a mol. wt. of 36,562. The predicted amino acid sequence had a high similarity with those from fungus A. chrysogenum and actinomycetes Streptomyces clavuligerus. The pcbC gene was expressed in E. coli and in A. chrysogenum under control of the tac and GAP promoters, resp.

L11 ANSWER 44 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:521776 HCAPLUS
DOCUMENT NUMBER: 123:26923
TITLE: Cluster of genes related to the biosynthesis of cephamycin C and lactam resistance in actinomycetes

AUTHOR(S): Liras, Paloma; Coque, Juan J. R.; Garcia-Calzada, Javier; Llarena, Francisco J.; Cardoza, Rosa E.
CORPORATE SOURCE: Facultad Biologia, Univ. Leon, Leon, 24071, Spain
SOURCE: Microbiologia (Madrid) (1994), 10(1y2), 49-56
CODEN: MICBE3; ISSN: 0213-4101
PUBLISHER: Garsi
DOCUMENT TYPE: Journal
LANGUAGE: Spanish

AB Three genes related to .beta.-lactam resistance have been found in the cluster of genes for cephamycin C biosynthesis in Nocardia lactamdurans. The cmcT gene encodes a hydrophobic protein located in the cytoplasmic membrane. The sequence of CMCT has a 21-31% identity in amino acids to proteins involved in antibiotic export from other antibiotic producing microorganisms. The pbp gene encodes a penicillin binding protein. Nocardia lactamdurans is rather sensitive to penicillins, but not to cephalosporins or cephamycin C. A third gene, bla, encodes a type A .beta.-lactamase. Both the .beta.-lactamase and the PBP protein, might form a system for the sensing and hydrolysis of penicillin intermediates which are released into the medium during the lysis of antibiotic producing cells.

L11 ANSWER 45 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:647794 HCAPLUS
DOCUMENT NUMBER: 121:247794
TITLE: A common system controls the induction of very different genes. The class-A .beta.-lactamase of Proteus vulgaris and the enterobacterial class-C .beta.-lactamase
AUTHOR(S): Datz, Martina; Joris, Bernard; Azab, Essam A. M.; Galleni, Moreno; Van Beeumen, Jozef; Frere, Jean-Marie; Martin, Hans H.
CORPORATE SOURCE: Inst. Chim., Univ. Liege, Belg.
SOURCE: European Journal of Biochemistry (1994), 226(1), 149-57
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Among the Enterobacteriaceae, Proteus vulgaris is exceptional in the inducible prodn. of a 29-kDa .beta.-lactamase (cefuroximase) with an unusually high activity towards the .beta.-lactamase-stable oximino-cephalosporins (e.g. cefuroxime and cefotaxime). Sequencing of the corresponding gene, cumA, showed that the derived CumA .beta.-lactamase belonged to the mol. class A. The structural gene was under the direct control of gene cumR, which was transcribed backwards and whose initiation codon was 165 bp away from that of the .beta.-lactamase gene. This resembled the arrangement of structural and regulator genes ampC and ampR of the 39-kDa mol.-class-C .beta.-lactamase AmpC present in many enterobacteria. Moreover, cloned genes ampD and ampG for neg. modulation and signal transduction of AmpC .beta.-lactamase induction, resp., were also able to restore constitutively CumA overproducing and non-inducible P. vulgaris mutants to the inducible, wild-type phenotype. The results indicate that controls of the induction phenomena are equiv. for the CumA and AmpC .beta.-lactamase. Very different structural genes can thus be under the control of identical systems.

L11 ANSWER 46 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:624949 HCAPLUS
DOCUMENT NUMBER: 121:224949

Search completed by David Schreiber 308-4292

TITLE: Gene sequence and biochemical characterization of FOX-1 from Klebsiella pneumoniae, a new AmpC-type plasmid-mediated .beta.-lactamase with two molecular variants

AUTHOR(S): Gonzalez Leiza, Marina; Perez-Diaz, Jose C.; Ayala, Juan; Casellas, Jose M.; Martinez-Beltran, Jesus; Bush, Karen; Baquero, Fernando

CORPORATE SOURCE: Servicio de Microbiologia, H. Ramon y Cajal, Madrid, 28034, Spain

SOURCE: Antimicrobial Agents and Chemotherapy (1994), 38(9), 2150-7
CODEN: AMACCQ; ISSN: 0066-4804

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Klebsiella pneumoniae BA32, a clin. isolate from Buenos Aires, Argentina, was found to produce a plasmid-encoded .beta.-lactamase (FOX-1) which conferred resistance to broad-spectrum cephalosporins and cephamycins. Resistance could be transferred by conjugation or transformation into Escherichia coli K-12 via a 48.5-kb plasmid (pGLK1) that produced two FOX-1 mol. variants with isoelec. points of 6.8 and 7.2 and apparent mol. sizes of 37 and 35 kDa, resp. The kinetic study revealed that the two variants had very similar substrate and inhibition profiles. These values resemble those of chromosomally mediated class C (group 1) cephalosporinases. The structural gene of FOX-1 (blaFOX-1) was cloned into a 2,270-bp PstI-PstI fragment and was expressed in E. coli TG1. The deduced 382-amino-acid sequence of FOX-1 exhibited a high degree of similarity with chromosomally encoded AmpC .beta.-lactamases of Pseudomonas aeruginosa, Serratia marcescens, Enterobacter cloacae, E. coli, and Citrobacter freundii. These findings suggest that FOX-1 is a plasmid-mediated AmpC-type .beta.-lactamase that is encoded by a single gene and that has two mol. variants.

L11 ANSWER 47 OF 60 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1994:597326 HCAPLUS

DOCUMENT NUMBER: 121:197326

TITLE: Analysis of a carbapenem-hydrolyzing class A .beta.-lactamase from Enterobacter cloacae and of its LysR-type regulatory protein

AUTHOR(S): Naas, Thierry; Nordmann, Patrice

CORPORATE SOURCE: Abteilung Mikrobiologie, Biozentrum der Universitat Basel, Basel, 4056, Switz.

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1994), 91(16), 7693-7
CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Carbapenems such as imipenem are extended-spectrum .beta.-lactam antibiotics, which are not hydrolyzed by the .beta.-lactamases commonly found in Enterobacteriaceae. Here the authors report a gene encoding a carbapenemase, which was cloned from the chromosome of a clin. isolate of Enterobacter cloacae, strain NOR-1, into pACYC184 plasmid in Escherichia coli. Unlike all the sequenced carbapenemases, which are class B metallo-.beta.-lactamases, the mature protein (NmcA) is a class A serine .beta.-lactamase, NmcA shares the highest amino acid identity (50%) with the extended-spectrum class A .beta.-lactamase MEN-1 from E. coli. In the opposite orientation from the nmcA promoter, an overlapping and divergent promoter was detected, along with an open reading frame, which encoded a 33.5-kDa protein (NmcR). The NmcR amino acid sequence displays homol. with LysR-type transcriptional regulatory proteins, including the

conserved residues near its N terminus within a helix-turn-helix motif. Deletion of nmcR resulted in decreased carbapenem resistance and a loss of .beta.-lactamase inducibility, demonstrating a pos. role of NmcR in NmcA expression.

L11 ANSWER 48 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:528674 HCAPLUS
DOCUMENT NUMBER: 121:128674
TITLE: Replacement of Serine 237 in Class A .beta.-Lactamase of Proteus vulgaris Modifies Its Unique Substrate Specificity
AUTHOR(S): Tamaki, Mami; Nukaga, Michiyoshi; Sawai, Tetsuo
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Chiba University, Chiba, 263, Japan
SOURCE: Biochemistry (1994), 33(33), 10200-6
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The chromosomal .beta.-lactamase gene of Proteus vulgaris K1 was cloned and sequenced. The gene comprises 813 nucleotides and codes for the mature enzyme of 29,655 Da, comprising 271 amino acids. The K1 .beta.-lactamase showed 30-70% similarity, in the overall amino acid sequence, to class A .beta.-lactamases of Gram-neg. bacteria. However, the K1 .beta.-lactamase differs from most class A enzymes in having a unique substrate specificity as a cephalosporinase, its spectrum extending to even oxyiminocephalosporins. To clarify the relationship between its unique substrate specificity and specific amino acid residues, alignment of the amino acid sequence of the K1 .beta.-lactamase with those of class A.beta.-lactamases was performed, and Ala104 and Ser237 were found to be candidates. Ala104 and Ser237 were replaced with glutamic acid and alanine, resp., which are commonly found in other class A .beta.-lactamases. The substitution at position 104 had no effect on the enzyme activity or the substrate specificity. The amino acid replacement at position 237, however, reduced the kcat/Km value for an oxyiminocephalosporin (cefuroxime) to 17% of that in the case of the wild-type enzyme, whereas the mutant enzyme showed a higher kcat/Km value for benzylpenicillin, 3 times, than that of the wild-type enzyme. These results indicated that Ser237 is one of the residues responsible for the unique substrate specificity of the P. vulgaris .beta.-lactamase.

L11 ANSWER 49 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:528649 HCAPLUS
DOCUMENT NUMBER: 121:128649
TITLE: Cloning and sequence analysis of the gene for a carbapenem-hydrolyzing class A .beta.-lactamase, Sme-1, from Serratia marcescens S6
AUTHOR(S): Naas, Thierry; Vandel, Laurence; Sougakoff, Wladimir; Livermore, David M.; Nordmann, Patrice
CORPORATE SOURCE: Abt. Mikrobiol., Univ. Basal, 4056, Switz.
SOURCE: Antimicrobial Agents and Chemotherapy (1994), 38(6), 1262-70
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Serratia marcescens S6 produces a pI 9.7 carbapenem-hydrolyzing .beta.-lactamase that is probably encoded by the chromosome. A total of 11.3 kb of genomic DNA from this strain was cloned into plasmid pACYC184 in Escherichia coli. After further subclonings, the carbapenem-hydrolyzing .beta.-lactamase gene (blaSme-I) was sequenced (EMBL accession

no. Z28968). The gene corresponded to an 882-bp open reading frame which encoded a 294-amino-acid polypeptide. This open reading frame was preceded by a -10 and a -35 region consistent with a putative promoter sequence of members of the family Enterobacteriaceae. This promoter was active in E. coli and S. marcescens, as demonstrated by primer extension anal. N-terminal sequencing showed that the Sme-1 enzyme had a 27-amino-acid leader peptide and enabled calcn. of the mol. mass of the mature protein (29.3 kDa). Sequence alignment revealed that Sme-1 is a class A serine .beta.-lactamase and not a class B metalloenzyme. The earlier view that the enzyme was zinc dependent was discounted. Among class A .beta.-lactamases, Sme-1 had the greatest amino acid identity (70%) with the pI 6.9 carbapenem-hydrolyzing .beta.-lactamase, NMC-A, from Enterobacter cloacae NOR-1. Comparison of these two protein sequences suggested a role for specific residues in carbapenem hydrolysis. The relatedness of Sme-1 to other class A .beta.-lactamases such as the TEM and SHV types was remote. This work details the sequence of the second carbapenem-hydrolyzing class A .beta.-lactamase from an enterobacterial species and the first in the genus Serratia.

L11 ANSWER 50 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:474885 HCAPLUS
DOCUMENT NUMBER: 121:74885
TITLE: Transcription and expression analysis, using lacZ and phoA gene fusions, of Mycobacterium fortuitum .beta.-lactamase genes cloned from a natural isolate and a high-level .beta.-lactamase producer
AUTHOR(S): Timm, J.; Perilli, M. G.; Duez, C.; Trias, J.; Orefici, G.; Fattorini, L.; Amicosante, G.; Oratore, A.; Joris, B.; et al.
CORPORATE SOURCE: Unite Genet. Mycobact., Inst. Pasteur, Paris, 75724, Fr.
SOURCE: Molecular Microbiology (1994), 12(3), 491-504
CODEN: MOMIEE; ISSN: 0950-382X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The gene encoding a class A .beta.-lactamase was cloned from a natural isolate of Mycobacterium fortuitum (blaF) and from a high-level amoxicillin-resistant mutant that produces large amts. of .beta.-lactamase (blaF*). The nucleotide sequences of the two genes differ at 11 positions, including two in the region upstream from the coding sequence. Gene fusions to Escherichia coli lacZ and transcription and expression anal. of the cloned genes in Mycobacterium smegmatis indicated that high-level prodn. of the .beta.-lactamase in the mutant is mainly or wholly due to a single base pair difference in the promoter. These analyses also showed that transcription and translation start at the same position. A comparison of the amino acid sequence of BlaF, as predicted from the nucleotide sequence, with the detd. N-terminal amino acid sequence indicated the presence of a typical signal peptide. The fusion of blaF (or blaF*) to the E. coli gene phoA resulted in the prodn. of BlaF-PhoA hybrid proteins that had alk. phosphatase activity. These results demonstrate that phoA can be used as a reporter gene for studying protein export in mycobacteria.

L11 ANSWER 51 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:402176 HCAPLUS
DOCUMENT NUMBER: 121:2176
TITLE: Characterization of a plasmid-borne and constitutively expressed blaMOX-1 gene encoding AmpC-type .beta.-lactamase

Search completed by David Schreiber 308-4292

AUTHOR(S): Horii, Toshinobu; Arakawa, Yoshichika; Ohta, Michio; Sugiyama, Tsuyoshi; Wacharotayankun, Rochaporn; Ito, Hideo; Kato, Nobuo
CORPORATE SOURCE: Sch. Med., Nagoya Univ., Nagoya, 466, Japan
SOURCE: Gene (1994), 139(1), 93-8
CODEN: GENED6; ISSN: 0378-1119
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A 1954-bp DNA fragment contg. the blaMOX-1 gene, identified on a large resident plasmid (pRMOX-1) of Klebsiella pneumoniae NU2936, was sequenced and an open reading frame (ORF) coding for a 390-amino-acid (aa) MOX-1 was found. The total deduced aa sequence of MOX-1 shared considerable homol. with that of AmpC-type class C .beta.-lactamases of Gram- bacteria, esp. of Pseudomonas aeruginosa PAO1 [51.3%; 63.8% at the nucleotide (nt) level]. However, the regulatory gene ampR and a 38-bp AmpR-binding region were not present upstream from blaMOX-1, although the expression of P. aeruginosa ampC is directly regulated by AmpR. Possible -35 and -10 regions, a Shine-Dalgarno (SD) sequence and terminators were identified which are peculiar to blaMOX-1. On the other hand, a sequence highly homologous (91.6%) to the region upstream from dhfrX in the In7 integron carried by plasmid pDGO100 was found upstream from blaMOX-1 at nt 1 to 488. No significant difference was detected between the promoter activities of blaMOX-1 in ampD- and ampD+ strains of Enterobacter cloacae, as measured by the chloramphenicol acetyltransferase (CAT) assay. These results clearly show that blaMOX-1 belongs to the group of ampC-related bla genes and that it is expressed constitutively, independently of transcriptional regulators such as AmpR, AmpG and AmpD. Homol. anal. among AmpC enzymes or ampC genes implied that integration of the chromosomal ampC gene into a large resident plasmid, followed by transconjugation, was involved in the evolution of blaMOX-1.

L11 ANSWER 52 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:656510 HCAPLUS
DOCUMENT NUMBER: 119:256510
TITLE: Recombinant (beta)-lactamase usable as carrier molecule for the preparation of immunogenic compositions
INVENTOR(S): Gicquel, Brigitte; Timm, Juliano; Trias, Joaquim; Duez, Colette; Perilli, Mariagrazia; Dusart, Jean; Frere, Jean Marie
PATENT ASSIGNEE(S): Institut Pasteur, Fr.
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9317113	A1	19930902	WO 1993-FR151	19930212
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2687410	A1	19930820	FR 1992-1713	19920214
FR 2687410	B1	19941216		
EP 626013	A1	19941130	EP 1993-905393	19930212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 5830457	A	19981103	US 1994-284465	19941114
PRIORITY APPLN. INFO.:			FR 1992-1713	19920214

Search completed by David Schreiber 308-4292

WO 1993-FR151 19930212

AB The sequence of Mycobacterium fortuitum .beta.-lactamase gene BlaM is presented. Chimeric genes for fusion proteins comprising .beta.-lactamase or fragments thereof and an antigenic peptide or protein may be expressed in suitable host cells to provide recombinant, chimeric proteins which may be used in immunogenic compns. The chimeric gene for a .beta.-lactamase-p24gag fragment (of HIV-1) fusion was expressed in BCG. Upon immunization of mice with this recombinant microbe, a specific cellular immune response was obsd.

L11 ANSWER 53 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:644303 HCAPLUS
DOCUMENT NUMBER: 119:244303
TITLE: .beta.-Lactamase of Lysobacter enzymogenes: Cloning, characterization and expression of the gene and comparison of the enzyme to other lactamases
AUTHOR(S): Goras, Gregory J.; Au, Samson; Roy, Kenneth L.; von Tigerstrom, Richard G.
CORPORATE SOURCE: Dep. Microbiol., Univ. Alberta, Edmonton, AB, T6G 2E9, Can.
SOURCE: Journal of General Microbiology (1993), 139(6), 1245-52
CODEN: JGMIAN; ISSN: 0022-1287
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The gene for the periplasmic .beta.-lactamase of Lysobacter enzymogenes was isolated as part of a 1017 bp EcoRI fragment and the nucleotide sequence of the gene was detd. It has a G + C content of 71.5% and encodes a 27 amino acid signal sequence and the mature .beta.-lactamase of 276 amino acids which has a mass of 29,146 Da. The enzyme appears to be unique to L. enzymogenes but its amino acid sequence shows a high degree of homol. with the amino acid sequences of the lactamase from Citrobacter diversus and other Class A .beta.-lactamases. The .beta.-lactamase gene of L. enzymogenes was expressed in Escherichia coli using pUC118 as the vector. The prodn. of active .beta.-lactamase was highest after the active growth phase of the expression host and reached levels which were about three times higher than those obtained with L. enzymogenes.

L11 ANSWER 54 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:512145 HCAPLUS
DOCUMENT NUMBER: 119:112145
TITLE: Genetic and biochemical analysis of a novel ambler class A .beta.-lactamase responsible for cefoxitin resistance in Bacteroides species
AUTHOR(S): Parker, Anita C.; Smith, C. Jeffrey
CORPORATE SOURCE: Dep. Microbiol. Immunol., East Carolina Univ., Greenville, NC, 27858-4354, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1993), 37(5), 1028-36
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A clin. isolate of Bacteroides vulgatus was resistant to tetracycline, clindamycin, ampicillin, cephaloridine, cefoxitin, and other .beta.-lactam antibiotics except imipenem. .beta.-Lactam resistance was mediated by a membrane-assocd., clavulanate-sensitive cephalosporinase capable of degrading cephalosporins and penicillins. Cefoxitin also was degraded but at a slow rate. The cefoxitin resistance (Fxr) determinant was cloned from B. vulgatus genomic libraries that were prepd. in Escherichia coli

and then mated with Bacteroides fragilis for the identification of Fxr strains. Anal. of B. fragilis strains with the cloned Fxr determinant revealed the presence of a new .beta.-lactamase protein with the phys. and enzymic properties of the .beta.-lactamase found in the original B. vulgatus isolate. The .beta.-lactamase gene (cfxA) was subcloned on a 2.2-kb DraI-HindIII fragment, and the nucleotide sequence was detd. These results showed that cfxA encoded a protein of 321 amino acids and 35,375 mol. wt. Mutant strains in which the cfxA structural gene was disrupted by insertional inactivation lost both Fxr and .beta.-lactamase activity. Comparisons of CfxA with other .beta.-lactamases showed a relationship with the active-site serine .beta.-lactamases in the Ambler mol. class A, although CfxA had apparently diverged significantly. This was exemplified by the substitution in CfxA at 13 of 25 amino acid residues previously identified as being invariant in class A .beta.-lactamases. These results suggest that CfxA may represent a new class A homol. group which diverged very early.

L11 ANSWER 55 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:488312 HCAPLUS
DOCUMENT NUMBER: 119:88312
TITLE: Genetic studies of alkaliphilic Bacillus sp. No. 170
AUTHOR(S): Kato, Chiaki
CORPORATE SOURCE: Japan
SOURCE: Superbugs (1991), 233-7. Editor(s): Horikoshi, Koki; Grant, William D. Japan Sci. Soc. Press: Tokyo, Japan.
CODEN: 57KBAV
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The authors analyzed the nucleotide sequence of a 1.9 kb DraI-EcoRI fragment which was responsible for the lipopenicillinase gene of pEAP121 of alkaliphilic Bacillus. The DNA sequence and the deduced amino acid sequence were detd. There was a single open reading frame of 930 bp which could encode a polypeptide of 310 amino acids. A putative ribosome-binding site, an AAGAGG sequence that was complementary to the 3' end of B. subtilis 16 S rRNA, was obsd. upstream of the open reading frame.

L11 ANSWER 56 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:423531 HCAPLUS
DOCUMENT NUMBER: 119:23531
TITLE: Close amino acid sequence relationship between the new plasmid-mediated extended-spectrum .beta.-lactamase MEN-1 and chromosomally encoded enzymes of Klebsiella oxytoca
AUTHOR(S): Barthelemy, Michel; Peduzzi, Jean; Bernard, Herve; Tancrede, Cyril; Labia, Roger
CORPORATE SOURCE: Mus. Natl. Hist. Nat., CNRS, Paris, 75231, Fr.
SOURCE: Biochimica et Biophysica Acta (1992), 1122(1), 15-22
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Isolated from an Escherichia coli strain, MEN-1 is a plasmid-mediated .beta.-lactamase that confers resistance to methoxy imino third-generation cephalosporins. The protein purified to homogeneity was digested by trypsin, chymotrypsin and endoproteinase Asp-N. Amino acid sequence detns. of the resulting peptides gave rise to the alignment of the 263 residues of the .beta.-lactamase. From amino acid sequence comparison MEN-1 was found to share more than 72% identity with the chromosomally

mediated .beta.-lactamases of Klebsiella oxytoca. Therefore, MEN-1 is the first transferable extended-spectrum .beta.-lactamase which is not directly derived from the widespread TEMs or SHV-1 penicillinases with which it presents less than 39% identity.

L11 ANSWER 57 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:402110 HCAPLUS
DOCUMENT NUMBER: 119:2110
TITLE: Genes for a .beta.-lactamase, a penicillin-binding protein and a transmembrane protein are clustered with the cephamycin biosynthetic genes in Nocardia lactamdurans
AUTHOR(S): Coque, Juan Jose R.; Liras, Paloma; Martin, Juan F.
CORPORATE SOURCE: Fac. Biol., Univ. Leon, Leon, 24071, Spain
SOURCE: EMBO Journal (1993), 12(2), 631-9
CODEN: EMJODG; ISSN: 0261-4189
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Three genes encoding a typical .beta.-lactamase, a penicillin-binding protein (PBP4) and a transmembrane protein are located in the cluster of cephamycin biosynthetic genes in N. lactamdurans. The similarity of the N. lactamdurans .beta.-lactamase to class A .beta.-lactamases from clin. isolates supports the hypothesis that antibiotic resistance genes in pathogenic bacteria are derived from antibiotic-producing organisms. The .beta.-lactamase is secreted and is active against penicillins (including the biosynthetic intermediates penicillin N and isopenicillin N), but not against cephamycin C. The .beta.-lactamase is synthesized during the active growth phase, prior to the formation of three cephamycin biosynthetic enzymes. The PBP of N.lactamdurans is a low-Mr protein that is very similar to DD-carboxypeptidases of Streptomyces and Actinomadura. The pbp gene product expressed in Streptomyces lividans accumulates in the membrane fraction. By disruption of N. lactamdurans protoplasts, the PBP4 was shown to be located in the plasma membrane. Eight PBPs were found in the membranes of N. lactamdurans, none of which bind cephamycin C, which explains the resistance of this strain to its own antibiotic. A transmembrane protein encoded by the cmcT gene of the cluster also accumulates in the membrane fraction and is probably related to the control of synthesis and secretion of the antibiotic. A balanced synthesis of .beta.-lactam antibiotics, .beta.-lactamase and BPB is postulated to be crit. for the survival of .beta.-lactam-producing actinomycetes.

L11 ANSWER 58 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:242064 HCAPLUS
DOCUMENT NUMBER: 114:242064
TITLE: Cloning and expression of genes for cephalosporin biosynthesis-related enzymes of Lysobacter lactamgenus
INVENTOR(S): Kimura, Hiroyuki; Miyashita, Hideaki; Sumino, Yasuhiro
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 67 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02291274	A2	19901203	JP 1990-3762	19900110

Search completed by David Schreiber 308-4292

JP 2928884 B2 19990803
PRIORITY APPLN. INFO.: JP 1989-24710 19890201
AB The DNA related with the biosynthesis of Cephalosporin (I) are cloned from L. lactamgenus and expressed in Escherichia coli or fungi such as Acremonium chrysogenum. The DNA contg. 9 open reading frames encodes 6 enzymes for the biosynthesis of I and 3 other proteins. It was cloned from a genomic library of L. lactamgenus constructed of .lambda.Fix arm using the IPS gene of A. chrysogenum as a probe. Expression of some or all of the genes for I biosynthesis in E. coli, Pseudomonas putida and A. chrysogenum were shown.

L11 ANSWER 59 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:241473 HCAPLUS
DOCUMENT NUMBER: 114:241473
TITLE: Cloning, sequencing and analysis of the structural gene and regulatory region of the Pseudomonas aeruginosa chromosomal ampC .beta.-lactamase
AUTHOR(S): Lodge, Julia M.; Minchin, Stephen D.; Piddock, Laura J. V.; Busby, Stephen J. W.
CORPORATE SOURCE: Sch. Biochem., Univ. Birmingham, Birmingham, B15 2TT, UK
SOURCE: Biochemical Journal (1990), 272(3), 627-31
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The chromosomal gene from P. aeruginosa encoding .beta.-lactamase was cloned, sequenced, and compared with corresponding sequences of .beta.-lactamases from members of the Enterobacteriaceae. Upstream of the .beta.-lactamase gene is an open reading frame which is postulated to encode a regulatory protein, AmpR. A helix-turn-helix region in AmpR and a putative AmpR-binding site were identified.

L11 ANSWER 60 OF 60 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:1343 HCAPLUS
DOCUMENT NUMBER: 114:1343
TITLE: Nucleotide sequence of the Serratia marcescens SR50 chromosomal ampC .beta.-lactamase gene
AUTHOR(S): Nomura, Kazuhide; Yoshida, Tadashi
CORPORATE SOURCE: Shionogi Res. Lab., Shionogi and Co., Ltd., Osaka, 553, Japan
SOURCE: FEMS Microbiology Letters (1990), 70(3), 295-9
CODEN: FMLED7; ISSN: 0378-1097
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The S. marcescens SR50 chromosomal .beta.-lactamase gene (ampC) was cloned and sequenced. It contains 1128 nucleotides encoding a protein of 355 amino acids preceded by 21 amino acids which probably constitute the signal peptide. The mature protein has a predicted mol. mass of 38,901 Da. About 40% of the amino acid sequence was identical among AmpC .beta.-lactamases of S. marcescens, Citrobacter freundii OS60, Escherichia coli K12, and Enterobacter cloacae P99. All of these enzymes are highly similar around the active site serine at the position 59 of the mature enzyme.

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